THE TOXEMIAS OF PREGNANCY

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BY

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PREFACE

The toxemias of pregnancy constitute a group of complications of the period of gestation which, in so far as a true knowledge of their processes is concerned, is still largely in the realm of theory and speculation. Notwithstanding this fact a fairly rational understanding of this subject now obtains and this monograph will attempt a presentation of the facts and such particular deductions as may be of value in the diagnosis and treatment of these abnormalities of the pregnant state.

The views held regarding the toxemias of pregnancy have undergone decided modifications since the early assumption that they were due merely to aberrations in the function of the kidney or liver. It is now more generally acknowledged that we are dealing rather with metabolic disturbances and that the clinical manifestations with which we are familiar are merely the expressions of localized damage to the organism. In the present work it is proposed, after tracing the development of our knowledge of the subject, to take up the etiology, symptomatology, and pathology, including the more recent studies in the chemistry of the blood and urine. The section on the urine has been contributed by Dr. F. E. Sondern, of New York, and that on the blood by Dr. J. A. Killian, of New York, to both of whom I desire to express herewith my sense of obligation. The final section is devoted to treatment and prophylaxis with particular attention to the results accomplished by adequate prenatal care.

I desire to acknowledge an indebtedness to those medical friends and colleagues who have courteously favored me with many valuable illustrations from original sources or from their published papers and books. I hope that I have not neglected to give due credit in every instance to these in the text.

GEORGE W. KOSMAK

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CHAPTER I

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The task of writing a historical introduction to this subject is lightened by the usual procedure adopted by most medical writers of going back to the fathers of all things medical, Hippocrates and Galen, for the necessary beginnings. In their treatises as they have come down to us, we find numerous though rather confused references to the diseases recognized to-day as the toxemias of pregnancy. Such irregularities in the normal course of gestation as manifested by constitutional disturbances were usually attributed to retention of various "humours," and while distinct references are made both to excessive vomiting and convulsive seizures, there are no specific explanations offered as to their cause, nor definite recommendation for their treatment. That the more violent manifestation of the toxemias of pregnancy were recognized in the time of Hippocrates may be gathered from the fact that the derivation of our word "eclampsia" is from the Greek εκλαμπω, which, meaning "flash" and conveying the idea of a sudden onset, was used by this writer to designate a rapidly developing fever. We find the word revived by Sauvage, who employed the term in his writings and in a work published in 1796, Gehler, taking it from the latter, introduced it into German medical literature. It was not until the beginning of the last century, however, that "eclampsia" superseded the more general designation of

"convulsions" as an appellation descriptive of the principal symptom associated with this complication of pregnancy. The occurrence of gestation in epileptic women led to confusion which persisted for a long time and we find that many writers in the early part of the nineteenth century still regarded the convulsions in the latter months of pregnancy as epileptic seizures.

Occasional references are found in the Italian medical works of the Middle Ages, but it is not until the eighteenth century that we meet with well recognized descriptions of the toxemias of pregnancy. Mauriceau, writing in the latter part of the seventeenth century, presents certain definite notions of these disorders. He attributes intractable vomiting to the cessation of menstruation, which caused "corrupt humours cleaving to the insides of the stomach, which being impossible to be evacuated by so many preceding vomitings because they adhere so fast, must be purged away by stool; to effect which they need a dissolvent, which may be a gentle purge . . . In perturbations and dejections of the belly, and in spontaneous vomitings, if the matter be purged away, the patient finds ease and comfort; if not, the contrary . . . If the vomiting continues daily, almost without intermission, although the woman observes a good diet, and after she hath been reasonably purged, we must rest there, lest something worse happen, for which we may incur the blame; she being then in great danger of miscarriage. And when the hiccough takes them through emptiness proceeding from too much evacuation caused by these continual vomitings, it is very bad."

Amberg reported, in 1713, his observations on convulsions, which are interesting enough to be repeated in detail. He describes the case of a young lady twenty-six years of age "who had gone about one-half her time with child and had not yet been bled, was invaded with convulsions of the hands, feet, head, mouth, and cheeks, which terrified her greatly, and rendered her apprehensive of their being succeeded by an apoplexy or epilepsy." She consulted Dr. Amberg who prescribed as follows: "Phlebotomy in the arm immediately to eight ounces. A teaspoonful every morning of a 'nervous powder' to be repeated in the afternoon at four o'clock and at bedtime." The majority of the ingredients of this powder cannot be duplicated in the present-day pharmacopœia, but were evidently designed for their refrigerant and laxative effects. Amberg states that, after continuing these medicines for two days, she "perceived no more of her convulsions, and she was happily delivered of a healthful child."

Burton, in his essay *Towards a New System of Midwifery,* London, 1751, in the part devoted to the diseases of pregnant women, repeats the earlier contention that some of these disorders arise solely from the stoppage of the menstrual flux; others from the motions and bulk of the fetus, secundines and waters. He claims that the "stoppage of the menstrual flux causes vomiting, loss of appetite, nausea, faintings, vertigo, pains in the stomach, shortness of breath and cough, all of which generally abate about the third month of pregnancy, or sooner. From the second cause also proceed vomiting, shortness of breath, cough, incontinence and suppression of urine, and constipation. Likewise pains in the back and groin, varices, piles, and swellings of the legs, thighs and pudenda." "These vomitings," he states, "seem to be occasioned by various causes which require different methods of relieving them. First, they may be caused by too great a distention of the blood vessels, whereby the nerves may be so pressed as to occasion that convulsive motion of the diaphragm, stomach, bowels and abdominal muscles which we call vomiting. Secondly, the vomiting may be occasioned by the remains of undigested food, being either too great in quantity or by being too acrimonious." The second cause, he moreover observes, "may proceed from too great extension of the womb, which sometimes will rise over-high in the abdomen, especially in people whose bones that form the lower part of the hypogastric region, are too straight, or as it is commonly called 'straight-hipped' . . . The appetite very often, nay generally, is depraved from the beginning of pregnancy, for the blood vessels being so much distended, by pressing on the nerves may hinder their action, so as to prevent their use in causing the sensation of hunger. Sometimes also this may proceed from the little consumption of the humours, the vessels being full; whence nature has not as great a demand, as the child consumes so little; and as the mother seems to perspire less than usual, as appeared from the seeming heaviness and torpor, which pregnant women so often complain of."

An interesting reference to "convulsions and lethargy occurring in labor" is found in a treatise by Madame Le Boursier du Coudray, Chief Midwife of Paris, published in 1777.

"It sometimes happens that a woman will have convulsions before she goes into labour. If such an accident happens, a competent doctor or surgeon should be called, as the condition is dangerous to both mother and child, and a careful examination should be made to find

out just how they are doing. While awaiting this assistance, the patient should be bathed with pure water, and care should be taken that none of it be allowed to touch her face or her throat, as this will increase the violence of the convulsions, as will likewise spirituous liqueurs. If labor begins during the convulsion, and the child presents well, there is hope for the patient and delivery should be hastened as much as possible. If there be a bad presentation, or version must be done, this will serve to greatly increase the irritation of the nervous system already so greatly disturbed; therefore it is better to await patiently the course of nature . . . There is another state apt to prove fatal to the woman, that is when she falls into a lethargy; all the resources of the animal economy being exhausted, so that there is nothing left to assist her in giving birth to the child. Under these conditions it is necessary to make delivery as promptly as possible, as that is the sole hope of saving the mother's life. I have often found myself in both the situations above outlined, and having called in skilled and competent (medical) people, I am able to state that none of my mothers died, and I was able even to deliver some living children."

Hamilton, in his *Treatise on Midwifery,* published in Edinburgh in 1781, refers to the alteration in the blood in the pregnant state which may account for many of the symptoms of pregnancy; particularly the appearance of a general, and sometimes of a local, plethora. He believes, however, that "many of the symptoms appear to be entirely of the nervous kind, and not readily explicable . . . In the advanced states of pregnancy the pressure of the uterus on the surrounding parts produces many complaints." He refers to convulsions during pregnancy as possibly occurring in the early months, although more common in the latter months, and at the commencement of labor. He states that the "appearance of epileptic fits in pregnant women is frightful; the symptoms are alarming; and the event is always precarious, often fatal." It is interesting to note Hamilton's description of the prodromal stage of which he says "headache, intolerably violent, or tense pain or oppression about the præcordia, are the most common presaging symptoms." The exciting cause he believes to be "uterine irritability communicated by sympathy to the encephalon, in some instances probably originating from the struggle or convulsive motions of the fetus, arising from its awkward or hampered position, and pressure of the gravid uterus interrupting the circulation through the abdominal viscera, disturbing their func-

tions and changing the determination both of the circulating fluid and nervous energy." Hamilton, it is stated in a footnote by Dr. Burns, was among the first English writers to employ the term "eclampsia."

In an English book by S. H. Jackson published in London, 1801, entitled *Cautions to Women Respecting the State of Pregnancy*, the writer, in describing the irritations of the stomach, claims that it would be nearer the truth "if we suppose them to arise either from pressure against the inside of the liver and gall-bladder, or on the great vessels belonging to the heart. This pressure is most likely to occur in persons of small stature and it is not infrequently accompanied by some degree of jaundice."

In the early years of the nineteenth century we begin to find more clear-cut references to hyperemesis and eclampsia. In Heath's *Translation of Baudelocque's Midwifery*, published in Philadelphia in 1807, puerperal convulsions are stated "to depend on sudden and great emotions of the mind, or a sanguine plethora, or an excessive flooding, or on a fullness of the primæ viæ, on an extreme sensibility of the uterine fibers, a violent distention of the edge of the orifice of the uterus, and of the parts which form the entrance of the pudendum. . . . The occurrence of all these causes is not necessary to produce convulsions; a single one is sufficient. All convulsions are not of the same nature nor affect the organs, nor equally disturb the harmony of the functions. Sometimes they present a frightful spectacle, at other times the countenance is tranquil. Sometimes the understanding does not return for hours or even days after these convulsions."

In Bard's *Compendium of Midwifery*, published in New York in 1815, we find extended references to hyperemesis and convulsive seizures. The writer insists that in intractable cases of vomiting relief is obtained only from a removal of five to six ounces of blood for three or four successive days rather than at one time. In accordance with the belief prevailing at that date he describes the convulsions of the latter months of pregnancy as "epileptic fits" to which women are peculiarly subject in pregnancy. He also states that "women who are inhabitants of populous cities and in the higher spheres of life, who have been delicately bred and who indulge themselves in a dissipated and luxurious life, are much more liable to these dreadful and fatal diseases than the more hardy inhabitants of the country, or than such as from constant labor and exercise enjoy robust constitutions." This scarcely agrees with our observation of the present day that eclampsia is as prevalent among the poor as among the well-to-do. It

is probably even more prevalent among the poor, unless proper supervision is maintained.

Bard believes, moreover, that "women are most liable to convulsions at the commencement of labor when the first dilatation of the extremely sensitive os uteri seems to bring them on. They are more apt to occur in a first, than in subsequent labors, from the great apprehension and terror which some women suffer on that occasion; and perhaps for a similar reason, whose labor is brought on by some dangerous accident, some sudden stroke of affliction, who have suffered convulsions on a former occasion, and those unhappy women, who, instead of rejoicing in the birth of the child, dread consequent reproach more than the pain and danger."

Further interesting observations are contained in the paragraph in which Bard states that "the danger of convulsions is in general in proportion to the advanced state of pregnancy, except when they occur after labor pains have begun, when a speedy delivery frequently carries them off; in other respects the danger is to be estimated more from the health and constitution of the patient, from the violence of the fits and from the stupor and apoplectic symptoms by which they are succeeded, than from the frequency of their recurrence. When each succeeding fit is more violent, and when they leave the patient more and more comatose, the danger is most imminent."

The conceptions held at the beginning of the last century on the toxemias of pregnancies are clouded by the interpretation which these writers placed on clinical symptoms. Thus, John Burns, a lecturer on midwifery in the medical school at Glasgow, designates by the term "febrile state," a train of symptoms now recognized as purely toxic in character. He believes that in such cases it is merely necessary to keep the bowels open and to take away a little blood. Burns also describes another so-called "species of fever" which affects women about the middle of pregnancy and makes its attacks suddenly like a "regular paroxysm of ague." The patient complains of headache, loathing for food, foul, dry tongue, considerable thirst, and is constipated. He states that the disease is very obstinate and often ends in abortion, after which, if the women do not sink speedily, they begin to recover but remain long in a "chlorotic state which, if not relieved, may terminate in phthisis." He even suspects that this disease originates from the bowels and bears a "great analogy to infantile remitting fever."

Burns, in another chapter, refers to headache as an alarming symp-

tom and in connection with the same describes very satisfactorily the syndrome now known as the pre-eclamptic stage, characterized by giddiness, visual disturbances, etc. In such circumstances, he says, "she is seized with apoplexy or epilepsy," and believes that these diseases are to be prevented by immediate recourse to bloodletting and laxatives. The quantity of blood which is to be removed must be determined by the severity of the symptoms, the habit of the patient, and the effect of the evacuations. If the headache is accompanied with edema, digitalis is recommended as a useful addition to the treatment. Burns also states that "if the patient is seized with apoplexy there is seldom any attempt made to expel the child; whereas in epilepsy if the paroxysm be protracted, the child may be expelled if the patient be not early cut off by a fatal coma. In some instances palsy either succeeds an apoplectic attack or follows headache and vertigo. This disease does not commonly go off until delivery takes place, but it may be prevented from becoming severe by mild laxatives and light diet."

In describing edema associated with pregnancy Burns mentions the severe cases in which "epilepsy" may result. When the edema is severe it may be attended with convulsions or it may predispose to puerperal disease, and he therefore insists that the edema must be reduced by bloodletting and purgatives.

The subject of vomiting in pregnancy is described by Burns in a very interesting manner, especially his reference to the necessity in severe cases of having the patient refrain from eating and giving her nourishing "clysters." Moreover, if the vomiting is bilious and accompanied with pains in the right side and shoulder, cough, and other symptoms of hepatitis, a seton should be immediately introduced into the side and a very gentle course of mercury given. If the vomiting becomes troublesome at the end of pregnancy "it is proper to detract blood and confine the patient to bed. Cloths dipped in laudanum should be applied to the pit of the stomach and a grain of solid opium given internally." But he does not say anything about induction of abortion in such cases nor mention the possible fatal result.

The subject of eclampsia is also dealt with by Burns in the chapter on complicated labor, in which he states that convulsions of various kinds may occur either during pregnancy or labor. One species is the consequence of great exertion, excessive fatigue, tedious labor, or profuse hemorrhage. The attack comes on without much warning and generally terminates with delirium. The muscles about the face and chest are chiefly affected and the pulse is small, compressible, and fre-

quent, the face pale, the eyes sunk, the extremities cold. The fits succeed very quickly and soon terminate in a fatal syncope. In treating the condition he refers to the necessity of keeping the patient quiet, and says that opium is of great service and that delivery is usually necessary. He also describes hysterical convulsions as more common during gestation than during labor. In these cases there is no foaming at the mouth, no working with the tongue, etc. The most frequent species of puerperal convulsions, however, is epileptic, which occurs fifty times for once that the other appears. Convulsions may affect the patient suddenly and severely, at stool or sitting in a chair. Presently, he says, the convulsion ends in a short stupor from which the woman awakes unconscious of having been ill, but in a short time the same scene is generally repeated; or, perhaps, although the convulsions have gone off, the stupor remains. It is not, however, unusual for the fit to be preceded by some symptoms which, to the attentive observer, indicate its approach. These are headache, pain in the stomach with unsupportable sickness, ringing in the ears, dazzling of the eyes or appearance of substances floating before them, slow pulse, and drowsiness during the pains.

How well the above description fits our modern conception of an eclamptic seizure, although we do not recognize the distinction between "hysterical epilepsy and the other convulsions." It is very likely that most of the cases of epilepsy or hysterical convulsions observed by the author were true eclamptic seizures. He admits that they are dependent on the pregnancy but goes no farther in advancing any theory as to their causation. Burns' directions for treatment are interesting. In the first place he cautions against injuries to the tongue and advises the insertion of a piece of wood between the teeth. Next the patient should be bled, or, when this cannot be done, further cupping in the temples and back part of the neck must be tried. If the convulsions recur the bleeding may be repeated, and he believes there is more danger from taking too little blood than from copious evacuations. From forty to eighty ounces of blood were taken from some of these cases of puerperal convulsions. He insists that bloodletting tends to relax the os uteri. After this a "smart clyster is given. The head is then shaved and blistered, the blister being proper though the fit have gone off." A small dose of calomel or solution of salts may also be given with advantage when the patient can swallow. The bladder must likewise be emptied, for its distention may cause convulsions. An interesting observation is that the depletion reduces the risk

of "fatal oppression of the brain or extravasation of blood within the skull and that consequently the convulsion is mitigated." Termination of the labor is advocated, which is favored by the bloodletting. The dilatation of the cervix by the hand should be resorted to and the child delivered with as little violence as possible. Burns believes that the use of medicaments, such as opium, musk and camphor, is not advisable without resort to the other procedures. If the patient is seen before the fits have occurred, preventive treatment includes emptying the bowels, use of an emetic and, in the presence of violent pains in the stomach, doing a venesection and giving an opiate. The appearance of headache also calls for the use of the lancet. Purgatives, he concludes, are a very important part of the treatment, and he has had better results from this than other methods, which makes him incline to the belief that an "incorrect state of the bowels is one of the most powerful predisposing causes of puerperal convulsions, and may also be the chief exciting cause."

James Blundell, in his *Principles and Practice of Obstetrics* (Am. ed. 1834), devotes considerable space to the subject of convulsions, and the following extracts from his book are of interest. Thus he says:

"Where convulsions do not actually occur there is sometimes a very obvious tendency to the attack, flushing of the face, throbbing of the carotids, severe pains in the head, and sensations of the brain, as if it were too large for its receptacle, which, indeed, in a certain sense, it is, in consequence of the blood flowing into it too copiously."

"Unhappily for the safety of the patient, she may be seized without premonitory symptoms; still, however, premonitory signs sometimes occur. Tremors of the whole muscular system, shudderings, crampy pains in the region of the stomach, cerebral afflux of blood, flushing and tumidity of the face, throbbing of the carotid arteries, severe and splitting pains of the head, stammering, and perhaps failure of utterance, constitute some of the leading prognostics. Sometimes the patient becomes deaf, and more frequently her sight is affected, dazzled with light, or blinded. When the fit supervenes, the woman becomes entirely insensible, and, together with this insensibility, she has a violent commotion of the voluntary muscles. . . . When these attacks have continued . . . a few minutes . . . we find the patient recovering [but] sometimes the patient lies deaf or blind or incapable

of speaking . . . as if the sensorium had received some permanent injury.

"Causes of convulsions: The immediate causes are very obscure; they appear sometimes to depend upon a loaded state of the vessels of the brain; at other times the brain appears to be influenced by distant irritations, either in the uterus, or in the digestive organs, and again, in some cases, puerperal convulsions, are induced apparently by a peculiar irritability of the nervous system.

"That the uterine organs are in some way implicated is evident, from the convulsions being of a character . . . peculiar to the state of either pregnancy or parturition. Some writers assign three especial causes which may give rise to this disease, namely, general irritability of the constitution, irritability of the uterus from distension and an overloaded state of the system.

"The custom of manner of living, the seasons or climate, and the general state of the health of the patients, are not wholly undeserving of being classed among the causes of these convulsions.

"To persons prone to cerebral afflux, convulsions may occur in the middle and earlier months sometimes, but still more frequently in the end of pregnancy.

"When convulsions attack a patient in the progress of gestation, she may have a single fit only or several, the intervals being usually irregular and somewhat long, not of a few minutes only, but of hours perhaps, or even days.

"Sooner or later, if the fit continues, parturition of itself commences. This can happen . . . in those cases also in which the disease is associated with apoplexy, so that during the whole time the woman is either comatose or convulsed. . . . Be at the bedside, therefore, in these convulsive cases, and watch, for as the paroxysms return the labor may advance, and the fetus may suddenly emerge.

"Should you ask me, in what manner convulsions are produced, I should reply that the more probable and immediate cause of them is a pressure on the brain, and perhaps on the spinal marrow also. This pressure sometimes results from the effusion of blood, still more frequently from the effused water, and most frequently of all from mere congestion. . . . An increased action of the vessels produces an accumulation of blood in the genitals, in the wattles of birds, and in the breasts of women during suckling and . . . I think it is not improbable that in these convulsions and convulsive propensities of women, a cerebral congestion, with pressure and irregular circulation,

and an increased action of the carotid and vertebral arteries, have a large share in producing the disease.

"In the end of gestation women are sometimes attacked with apoplexy, in which condition they may be for hours or days, recovering gradually afterward or ultimately sinking. Under apoplectic attacks, I believe, labor does not so readily come on as under convulsive attack; nevertheless, I would advise you to examine the os uteri occasionally, and take care that the child is not born unperceived. In its nature, though there are no spasms, I look upon this disease as strictly analogous to the convulsions of which I have been speaking, and I would therefore, treat it upon the same principle."

I have quoted a certain number of historical references *in extenso* to show that the clinical knowledge of the toxemias of pregnancy has been in existence for several centuries and that methods of treatment now in use were then employed for similar purposes, including purging, venesection, and the administration of sedatives and alkalies. It is perhaps rather discouraging to be compelled to make an admission, in reviewing the history of this subject, that we have not made any noteworthy advances except in a better knowledge of associated pathology and the chemistry of the urine and, more recently, the chemistry of the blood. The clinical picture of an eclamptic seizure painted by Burns in 1811 is not, except for certain details, very far removed from that described in modern obstetrical textbooks. Nor have we determined with any degree even approximating to certainty, what are the precise etiological factors underlying the production of these various abnormalities in the pregnant state. This uncertainty regarding etiology makes our modern modes of treating hyperemesis, eclampsia and the other toxemias, largely empirical. For example, whether to resort in the treatment of eclampsia to immediate delivery, or to employ palliative measures is a question by no means settled, and arrays of facts and figures are presented by both groups of observers, radical and conservative, in defense of their individual claims. The incidence and the mortality of the toxemias of pregnancy still remains high, although recent years have witnessed great improvement, particularly in eclampsia, where preventive measures have undoubtedly proved their value. But there is much yet to be learned, and before us is a task worthy of the earnest attention of medical investigators, in which the combined thought and labor of clinician and laboratory worker, rather than either alone, must be brought to bear on the prob-

lem. It is problematical where the search will lead us and what epoch-making discovery will reveal one or more etiological factors that will serve as a basis for rational therapeutics. Or, perhaps, prophylaxis alone, as in so many other diseases, will point the way to an eradication of these serious complications of the pregnant state.

A condition so widespread and often so disastrous in its effects as the toxic disorders of pregnancy has been a stimulus to many workers, and medical literature is so crowded with references that it would be impossible to present them even in résumé within the limits of this volume. It has, therefore, seemed advisable to include under each subdivision a general descriptive account of the subject, followed by brief references to the more important original works, which are thus available for further reading and consultation.

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CHAPTER II

ETIOLOGY AND SYMPTOMATOLOGY

Autointoxication long considered the principal etiological factor—Disturbances in metabolism claimed to be basis of varying clinical manifestations of a single condition—This theory combated especially by Williams—Histologic, blood and urine studies indicate essential differences—No specific principles thus far isolated nor specific pathologic lesions recognized—Classification of pregnancy toxemias—Hyperemesis gravidarum, toxic and psychic factors—Hepatic lesions —Glycogen deficiency—Acute yellow atrophy of the liver—Differential diagnosis—Bacterial theory—Nephritic toxemia—"Kidney of pregnancy"—Symptoms—Specific toxic factor, as etiology—Pre-eclamptic toxemia—Difficult to draw distinction between this and former symptoms—Eclampsia—Definition— Frequency — Incidence — Influence of seasons — Mortality — Clinical course — Ante-, intra- and post-partum types—Severity—Eclampsia without convulsions —Peripheral nerve lesions—Blood pressure and its significance—Rôle of kidneys—Infections—Placental autolysis—Internal gland derangements—Exophthalmic goiter—Effect of thyroidectomy—Mammary gland theory—Anaphylactic reaction—Dissenting views on sensitization—Prognosis for mother and fetus — Influence of war diets — Differential diagnosis — Epilepsy — Chorea — Hysterical convulsions—Increased salivation—Presumable toxemias—Prognosis in toxemia—Literature.

Introductory.—It would be a difficult matter to discuss the etiological factors underlying the production of the so-called toxemias of pregnancy from any one point of view, for, as is now well known, the most divergent clinical manifestations may be accompanied by similar pathological features, and, to a certain extent, the reverse of this also holds good. For example, in the disorders of the later months of pregnancy to which the general term "eclampsia" is given, death may be the terminal manifestation of a series of symptoms marked by one or more convulsive seizures and may also constitute the final picture in a case in which no convulsions whatever occurred. Autopsies in each instance show practically the same pathological lesions in brain, liver, kidneys, and other organs. At first it was believed that abnormalities of the functions of liver and kidneys resulted in the retention of certain by-products of body metabolism which gave rise to a toxic state.

The earlier French observers particularly regarded a condition of autointoxication as present in almost all pregnancies and attributed a large variety of abnormal manifestations to the same process, including headache, skin eruptions, salivation, etc., as well as the more serious manifestations of the eclamptic seizures. Veit claimed that such disturbances resulted from the entrance of bits of villi originating in the fetal ectoderm which find their way into the maternal circulation and produce a cytolysis. Ewing, Stone, and others believed that the toxemias of pregnancy, including hyperemesis and eclampsia, were all evidences of disturbed metabolism and therefore should be regarded and treated as a single condition with varying manifestations.

J. Whitridge Williams combats this opinion very vigorously in his writings and states that the study of the urine and blood as well as the histological examinations of tissues indicates that essential and characteristic differences exist between the various conditions thus grouped together. He believes that the probability of the eventual discovery of their ultimate causes would be greatly increased by considering them separately. Moreover, no specific poisonous principles have been isolated to date, nor have any distinctive pathological lesions been recognized which could not be associated with other conditions.

The classification of pregnancy toxemias proposed by Williams is very satisfactory from the standpoint of our present knowledge of the underlying chemical or physiological factors, although the clinical distinctions between nephritic and pre-eclamptic toxemias, for example, may perhaps be difficult or doubtful in certain cases. Under the general heading of toxemia of pregnancy, Williams describes the following groups: (*a*) pernicious vomiting; (*b*) acute yellow atrophy of the liver; (*c*) nephritic toxemia; (*d*) pre-eclamptic toxemia; (*e*) eclampsia; (*f*) presumable toxemias. Adopting Williams' view, it will be necessary to consider the etiology of each group of cases because, as already stated, later pathological studies seem to point to the necessity of dividing the various toxemias in this manner. We must, however, still regard the problem as unsolved, for notwithstanding many theories that have been put forward to account for any and all of these abnormalities, none has been satisfactory enough to warrant its adoption as a basis for definite prophylaxis or treatment.

HYPEREMESIS GRAVIDARUM

Etiology.—Taking up first the vomiting of pregnancy, it will be found to occur in greater or less degree in over one-half of the cases, beginning at the end of the first month and continuing ordinarily until the third or the fourth month. The appearance of this symptom is so common that the term "morning sickness" is well known to all pregnant women. In many instances nausea alone appears and vomiting is absent, or only occasional. The gradations are numerous between this type of vomiting, which is usually regarded merely as a discomfort and the more serious conditions in which the vomiting actually leads to starvation, with its attendant results. The fact that nausea and, in many cases, vomiting, follow manipulations on the nonpregnant uterus (dilatation of the canal with gauze, with instruments, or stem pessaries) makes it possible that certain nerve adjustments are needed before the irritations from this source no longer elicit reflex gastric disturbances. On the other hand, a mere neurosis does not serve as an explanation because so many women of a markedly neurotic type fail to show any evidences of morning sickness, while others who manifest no tendency in this direction and are apparently robust and calm, may suffer excruciatingly from the same symptoms. Certain mechanical displacements of the uterus may be assumed to be a causal factor in certain cases, as the vomiting frequently disappears when they are corrected.

Toxic and Psychic Factors.—In addition to the neurotic or reflex types, a toxic element is most probably the predisposing cause in the majority of cases of hyperemesis; for the symptoms often persist where apparently reflex causes have been done away with. One may also assume that in such cases the mental effect resulting from the removal of a mechanical cause has a marked influence on the patient. In those cases where there is no true toxic factor, suggestive treatment has been employed on the supposition that a hysterical element was the underlying condition, and one becomes very much impressed by this view from the fact that a scheme of treatment in which absolute quiet and rest are set down as essential factors, often brings about a marked and immediate improvement in the patient.

High Ammonia Coefficient.—In the large majority of cases, however, it would be better to regard a toxemia as the true cause

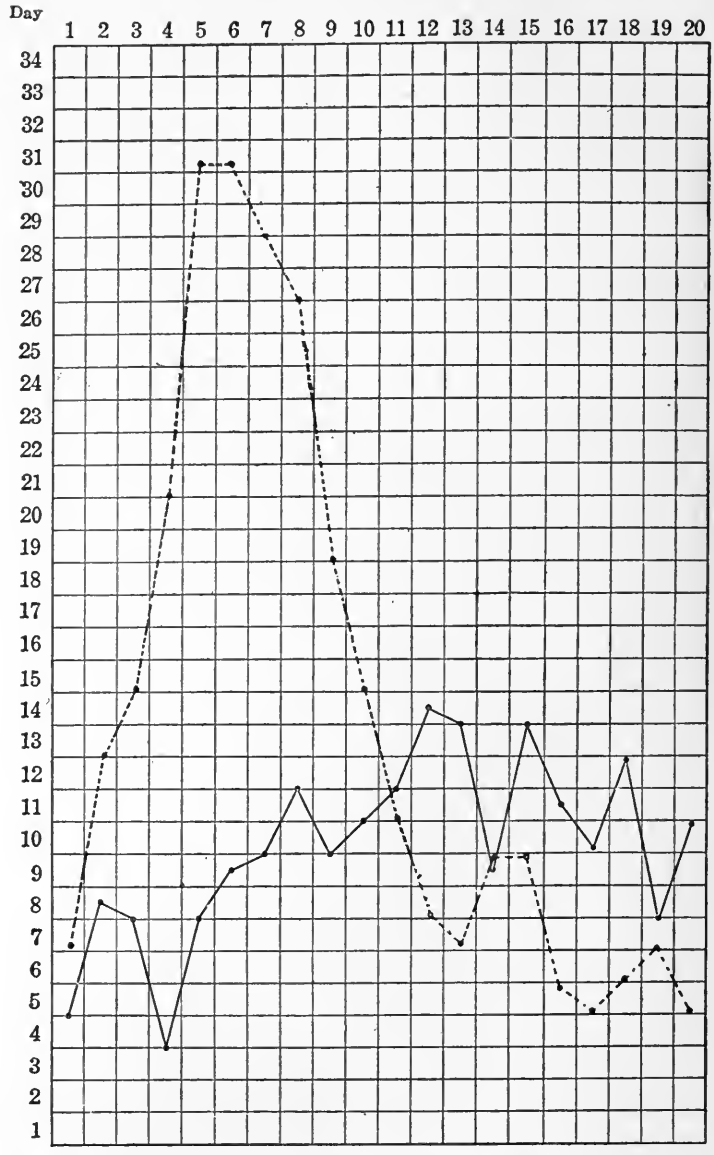

FIG. 1.—GRAPHIC CHART SHOWING URINARY CONDITIONS IN A CASE OF NEUROTIC VOMITING WITH STARVATION, CURED BY SUGGESTION AND FORCED FEEDING. Dotted line shows variations in ammonia coefficient. Continuous line shows grams of total nitrogen (Williams).

of the symptoms, but how can we distinguish the border-line cases and determine whether we are dealing with a true toxemia or a reflex disturbance? In the true toxemic cases there are evidences of disturbed metabolism in the blood and urine upon which a diagnosis may be based. Williams was the first to show that the urine in such patients presents a high ammonia coefficient, which indicates that a much larger proportion of the total nitrogen is excreted in the form of ammonia than usual. Normally the ammonia coefficient during pregnancy varies between 4 and 5 per cent, but in toxemic vomiting it may rise from 20 to 50 per

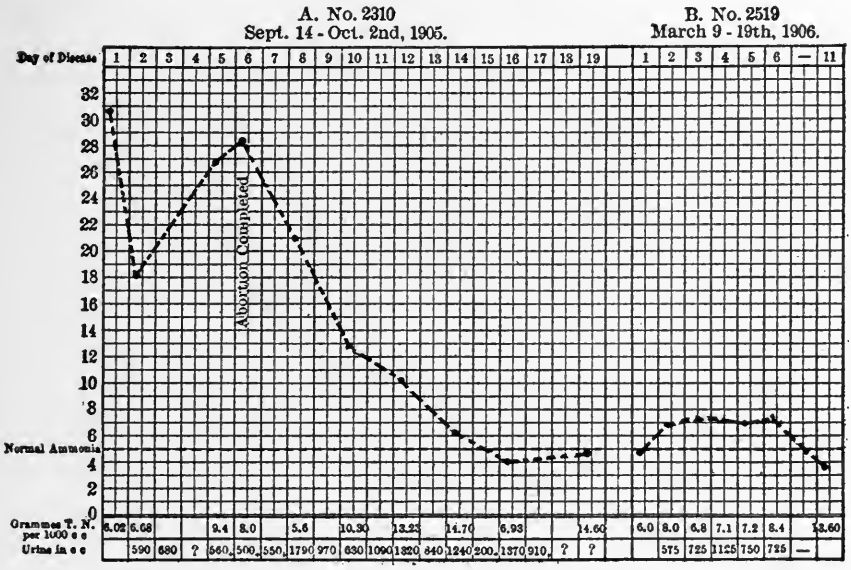

FIG. 2.—GRAPHIC CHART SHOWING AMMONIA COEFFICIENT IN TWO SUCCESSIVE PREGNANCIES. *A*, toxemic, and *B*, neurotic type of vomiting (Williams).

cent. These conditions are well shown in the accompanying charts from Williams' textbook (Figs. 1, 2). Williams insists that these findings indicate profound perversion of metabolism and are associated with grave danger to the patient. His statements, however, were later contradicted by those who believe that the high ammonia coefficient is a manifestation of acidosis, or merely an accompaniment of inanition and in no way connected with a toxemic process. Williams claims, however, that the high ammonia coefficient in women suffering from pernicious vomiting is not always susceptible to this explanation, because the employment of soda bicarbonate in his experience had no effect upon the

ammonia coefficient or upon the reaction of the urine, which would have been materially altered in a mere acidosis. Williams also denies that the high ammonia coefficient in all cases is due to inanition, as is clearly shown by the history of the patient whose urinalysis is presented in Fig. 3. Here the ammonia coefficient fell from 33 per cent to practically normal but the inanition continued and he explains this by assuming that the high ammonia coefficient was a manifestation of a toxemia which ceased as soon as the pregnancy which caused it was ended.

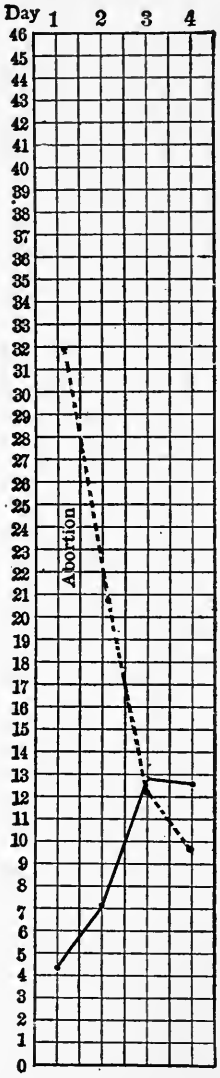

FIG. 3.—URINARY CHART FROM A CASE OF TOXEMIC VOMITING. With recovery after induced abortion, showing total nitrogen — continuous line — and ammonia coefficient — dotted line (Williams).

Hepatic Lesions. — That serious liver necrosis can be associated with hyperemesis was first pointed out by Duncan in 1879 and these observations were later confirmed by Williams, Stone and Ewing, who showed that in some cases a profound necrosis of the central portion of the lobules took place whereas the periphery remained intact (Fig. 4). In place of this necrosis, marked fatty degeneration may occur.

The lesions found in the kidney in patients dying from hyperemesis show degenerative changes in the convoluted tubules, including necrosis of the epithelium. Williams believes that the hepatic lesions are entirely different from those observed in eclampsia, in which the process begins in the periportal spaces and is primarily due to thrombosis; that toxemic vomiting is an entirely distinct process, and that it has only two points in common with eclampsia, namely, that both occur in pregnant women and are manifestations of disturbed metabolism. He declares further that it is probable that the extensive destruction of liver tissue may account for a part of the urinary changes, by so interfering with the intermediary stages of protein

metabolism that ammonia and other incompletely oxidized substances are excreted instead of urea. He also believes that when the distortion of the nitrogenous partition is not due to inanition, the greater part of the change must be attributed to the underlying toxemia concerning whose nature we are not well acquainted.[1]

The view that the liver lesions are due to chloroform poisoning was advanced by the opponents of this theory, but Williams has shown that the same lesions are observed after the employment of ether or nitrous oxide gas, and even in patients who died before any attempt at abortion had been made. He claims that there is abundant evidence to prove that certain cases of pernicious vomiting are due to a toxemia, which is associated with a high ammonia coefficient, a marked reduction in the output of urea, and with profound degenerative lesions of the liver and kidneys. Further, such a condition usually terminates in death unless the pregnancy is speedily terminated.

Glycogen Deficiency.—Duncan and Harding considered that the similarity in the symptoms of ordinary hunger and hyperemesis might account for the periodicity of the vomiting of pregnancy, and that the cause lies in a lack of glycogen in the liver which, they claim, leads to a fatty infiltration of that organ. Their aim was to correct the supposed deficiency of carbohydrates by means of a high carbohydrate diet supplemented by glucose or lactose, further reference to which may be found in the section on treatment.

ACUTE YELLOW ATROPHY OF THE LIVER

Etiology.—The etiology of acute yellow atrophy of the liver occurring in pregnancy as such is probably associated with the same series of deviations from the normal which underlie the other and better known varieties of toxemia of pregnancy. Whether to consider an acute yellow atrophy of the liver a clinical entity or merely the terminal lesion in any given case of hyperemesis or eclampsia cannot be determined without a knowledge of its etiology. This must be regarded as still uncertain. In some cases a predisposing cause may be found, such as pernicious vomiting,

[1] In this connection it may be noted that Mottram found that in the pregnancy of ill-nourished animals the liver became overloaded with fat just as in certain stages of ordinary inanition.

sepsis, eclampsia, typhoid fever, drug poisoning, intestinal auto-intoxication, wasting illness, etc., to mention the more commonly found conditions, but in other cases there is apparently no previous history of this kind. Collections of cases of acute yellow atrophy of the liver show that where it is found among women, anywhere from 50 to 60 per cent of these are pregnant, or have recently been delivered. In this connection it is important to note that jaundice may occur in pregnancy as an accidental symptom. It may be of the catarrhal variety or due to cholecystitis or cholelithiasis, and again, it may be of an idiopathic type in which all other etiological factors have been eliminated. In the latter instance we are dealing merely with a symptom complex marked by discoloration of the skin and sclera, by itching and nervous irritability. One of the characteristic features of this condition is its recurrence in the same or successive pregnancies. The cause of this form of pregnancy icterus has not been determined, but in view of the known effect on the liver cells of the toxins of pregnancy we may assume this to be one, if not the principal, etiological factor.

Differential Diagnosis.—But the symptom complex just described must be carefully distinguished from a true acute yellow atrophy of the liver, although this may be difficult, for a severe group of symptoms is gradually superimposed on the milder ones of the ordinary jaundice so often seen in pregnancy. Every case of persistent icterus occurring in pregnancy must be regarded with apprehension. Evidences of a more serious condition are to be found in the nausea and vomiting, more pronounced jaundice, coated tongue, dry skin, periods of depression alternating with delirium, and convulsive movements, usually of the extremities. Palpation shows a steadily enlarging, tender liver. Purpuric skin spots and the finding of leucin and tyrosin crystals in the urine usually precede the fatal issue. It may be difficult to draw a close clinical distinction between an actual acute yellow atrophy and hyperemesis, as marked degrees of jaundice often accompany the latter, but, while emptying the uterus often stops the vomiting, it has no effect on a true liver atrophy. It is probable, moreover, that many deaths from hyperemesis are really due to true atrophy of the liver which could be proved if autopsies were possible.

Bacterial Theory.—In addition to the predisposing causes already noted, the disease has been attributed to a bacterial origin,

both the streptococcus and colon bacillus having been isolated from the liver at autopsy. It has not been shown, however, that these are not secondary reinfections and the picture afforded by sections of the affected organ points to a degenerative rather than an inflammatory process.

NEPHRITIC TOXEMIA

The overburdening of the maternal kidney function during pregnancy undoubtedly serves as a starting-point for the frequent disorder to which the term "kidney of pregnancy" has been applied. In many instances an existing nephritis that can be traced to one of the exanthemata may undergo an exacerbation after years of quiescence. Every infectious disease may be complicated by nephritis during pregnancy and the prevalence of epidemic influenza during recent years, I believe, accounts for the increased number of the cases that have occurred lately. The presence of a chronic nephritis may be unknown to the patient and may make itself evident only during pregnancy, because of the increased burden placed upon the kidneys. The mere presence of albumin in the urine is not necessarily an indication of this lesion, as this may appear in minute quantities in the urine of perfectly healthy people and especially after severe exercise, but albuminuria characterized by more marked traces is associated with many pregnancies and constitutes a predisposing factor for a more serious involvement of the kidneys. In all cases where the albumen reaction averages 1 to 1,000, or more, we may assume that the normal limits have been exceeded, especially if this is accompanied by casts of the hyaline or granular variety.

Symptoms.—We find that the onset of nephritic toxemia is gradual in most instances, which serves to distinguish it from the renal symptoms in actual eclampsia. Appearing usually in the second half of pregnancy, it attacks primiparæ more often than multiparæ; it is also likely to be associated with multiple pregnancies. In addition to the urinary findings, edema of the ankles and legs is present in varying degrees and sometimes involves the lower portion of the abdomen. Puffiness and swelling of the hands is usually noted, although they may not be so evident as an edema. In a certain number of cases, headache, nausea, indigestion and slight visual disturbances are present.

It may be safely assumed that some direct and specific toxic factor is the exciting cause of this disturbance in the kidneys and not, as was formerly believed, a mechanical condition, such as that arising from increased intra-abdominal tension, heightened blood pressure or added muscular activity during labor. Functional kidney tests seem to show that in these cases the excretory possibilities for water and salt are considerably reduced. This would point to a retention of these materials in the organism with consequent ill effects. In many cases the progress of the kidney involvement is apparently halted at this stage and no further extension of the process results. In others the incidence of more advanced toxic symptoms indicates an extension of the process clinically into a pre-eclamptic toxemia or into an actual eclampsia.

There is another group of phenomena to which attention must be called. Williams, among others, has pointed out that women who give birth to premature infants repeatedly are likely to be the subjects of this condition. It will be noted in these cases that the patient is apparently well up to the middle of her pregnancy, when albuminuria, with an accompanying edema, appears. The patient goes into labor and gives birth to a poorly nourished infant or one that is stillborn. The children are poorly nourished because of the insufficient placental nutrition, the organ in these cases being diseased and the seat of infarcts.

PRE-ECLAMPTIC TOXEMIA

It may be difficult to draw a distinction between nephritic toxemia and that to which the term "pre-eclamptic toxemia" has been given and most cases are probably better labeled by the latter term. The clinical signs and symptoms show a marked resemblance to that class in which the kidney alone seems to play a leading part. A distinction may be made, however, in that the evidences of specific kidney lesions are less well defined and we may have presented simply the picture of a toxic disturbance. Pre-eclamptic toxemia usually comes on between the seventh and ninth month and may be associated with a varied train of symptoms. The milder cases are characterized by headache, malaise, a moderately high blood-pressure and more or less edema of the extremities. In the more severe cases pain in the epigastrium, persistent headache and visual disturbances (including spots

before the eyes, inability to read, or attacks of dizziness), are present. In some cases the patients suddenly find themselves unable to see and in other cases the loss of sight may come about more gradually. Mental disturbances are also frequent and the patient may present various types, ranging from irritability to a state which closely resembles insanity. In some cases sleeplessness is complained of, in others the patients are drowsy and stupid most of the time. Where the symptoms are not checked the condition may pass into eclampsia marked either by convulsions or a profound coma ending in death. A characteristic feature of this condition is the reduction in the amount of urine, which may be as low as ten to fifteen ounces in twenty-four hours, containing albumen, casts, and sometimes blood cells. As a rule the urine is highly acid, and acetone and diacetic acid may be present, although less marked than in other toxic manifestations.

ECLAMPSIA

Definition.—This term, as now employed, is limited to those acute manifestations of toxemia during the latter half of pregnancy, characterized usually by convulsive seizures after or between which there is a loss of consciousness. Recovery may follow one or more convulsions, or a state of coma ensues which, with other manifestations, may terminate in death. The term "eclampsia" is in a sense a misnomer, because we find in some instances that coma and death ensue without previous convulsions. As eclampsia constitutes one of the most serious complications of pregnancy a great deal of time and effort has been devoted to studies directed toward the solution of its cause or causes. A glance at the historical review will demonstrate that its character was known before the highly developed laboratory methods of the present day afforded more definite clues as to its etiology. Nevertheless the search must go on, and it is immaterial whether the clinician or the laboratory worker is successful. The predisposing causes, however, are now better understood and much has been accomplished by prophylactic measures in reducing the incidence and mortality of eclampsia.

Frequency.—The frequency of the occurrence of eclampsia has been variously estimated. Statistics derived from maternity hospitals show a considerable variation. Thus a report by

Williams in 1912, based on his service at the Johns Hopkins Hospital, shows an incidence of 1 per cent in a series of 11,000 labors; Lichtenstein, of Leipzig, in 1911, reports 400 cases of eclampsia in about 15,000 labors, or over 2.5 per cent. Reinburg, presenting a series of French statistics in his thesis, dated 1905, found an incidence of 0.34 per cent in a series of over 26,000 cases. Finally, McPherson reports in a recent unpublished communication, an occurrence of 890 eclampsias in 120,000 labors at the New York Lying-in Hospital, or a proportion of about 1 to 135 patients, or about 0.74 per cent. In presenting statistics based on hospital records it must be borne in mind, however, that they may be unduly exaggerated because of the large number of such patients that are necessarily referred to institutions for treatment.

Who Affected and Time.—Primiparæ are more apt to be affected by eclampsia than multiparæ, and both multiple pregnancies and hydramnios are generally assumed to be predisposing factors. Although associated, as a rule, with the later months of the pregnant period, cases have been repeatedly observed during the first half of pregnancy. In one instance a fatal case with convulsions was noted during the fourth month in which the autopsy showed rupture, cerebral hemorrhage and a chronic nephritis, together with characteristic changes in the liver. E. P. Watson also reports a case in a primipara twenty-five years of age who developed a gradual generalized edema, headache, and finally sudden coma following severe typical eclamptic convulsions at the fifth month. The urine boiled solid and contained granular casts. Vaginal section was done and twins delivered. Postpartum convulsions followed and the coma did not disappear for three days after delivery. Hemiplegia was present in this case for six days, but the patient finally recovered. Ebeler, in 1916, collected 50 cases of eclampsia occurring in the first half of pregnancy. We may find that eclampsia is associated with abnormal forms of gestation, including extra-uterine pregnancy and hydatidiform mole. Ebeler also reports the occurrence of eclampsia in a case of ruptured extra-uterine pregnancy in which the patient, after an amenorrhea of eight weeks, developed the usual signs of sudden internal hemorrhage. Operation was performed and a few hours later a slowly progressing coma developed, followed by listlessness and typical convulsions. The urine showed a large amount of albumen, together with numerous glandular and hyaline casts, and the

patient died soon afterwards. The same author refers to three similar cases which he collected from the literature.

Influence of Seasons.—The influence of the seasons on the incidence of eclampsia has several times been advanced as a possible factor in the production of this condition. Cold, damp, and unsettled weather, such as is often met with in the vicinity of New York during the early spring months, is attended by an increase in the number of eclampsia cases admitted to the hospitals. Harrar has shown this in a graphic manner. The accompanying diagram,

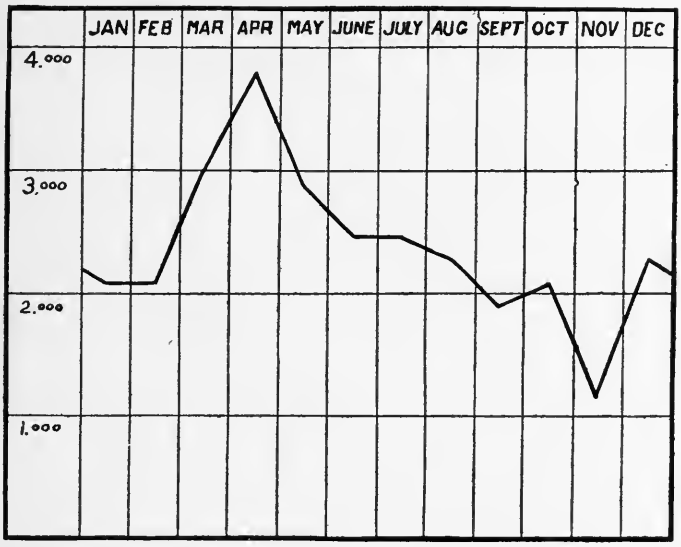

FIG. 4.—GRAPHIC CHART SHOWING THE INCIDENCE OF ECLAMPSIA IN DIFFERENT SEASONS. Based on a series of cases at the New York Lying-in Hospital (Harrar). The line depicts the number of cases per 100 deliveries.

(Fig. 4), which represents the cases of eclampsia occurring in the Lying-in Hospital of New York during a period of ten years, shows a steady increase in the number beginning in February and reaching its maximum in April. This is followed by a steady decline with a minimum number of cases reported during the month of November. The latter month, although usually cold, is characterized by a low rainfall. Others have denied this connection and claim that the association is entirely accidental. Statistics have also been brought forward by Hammerschlag to show that the disease is more prevalent in city than in country districts; but that the mortality is higher in the country, probably because of the inability to provide early and proper medical attention.

Mortality.—The mortality of eclampsia unfortunately remains high, being estimated at from 25 to 33 per cent and even more for the mother, and at from 33 to 60 per cent for the child. In recent years improvement in these high mortality rates has been noted, due unquestionably to better prophylaxis, a subject which will be discussed in the section on treatment. At the New York Lying-in Hospital the mortality record for recent years, in the in-door service, is shown in the following table:

INDOOR MORTALITY RECORD OF ECLAMPSIA CASES

Year	Total Number of Confinements	Deaths	Eclampsia Deaths
1910	2,041	62	11
1911	2,275	48	9
1912	2,521	56	12
1913	2,745	55	8
1914	3,060	68	15
1915	3,018	72	17
1916	3,214	50	11
1917	3,186	57	8
1918	4,010	75	8
1919	2,707	54	11
1920	2,798	42	9

For this same period the death rate from eclampsia in the Greater City of New York, taken from the records of the Municipal Health Department, are as follows:

MORTALITY RECORD FOR GREATER NEW YORK*

Year	Total Births	Maternal Deaths	Deaths from Eclampsia
1912	135,655	676	161
1913	135,134	668	171
1914	140,647	679	164
1915	141,256	710	144
1916	137,664	666	158
1917	141,564	651	169
1918	138,046	664	184
1919	130,377	644	171
1920	132,856†	708	190
1921	134,241‡	746	169

* The Statistical reports of the Department of Health of New York City refer to deaths from "convulsions" and "albuminuria," which are herewith considered to he synonymous with our general designation of eclampsia.

† Of these 6,234 were stillbirths. ‡ Of these 6,297 were stillbirths.

The hospital figures are high, because the institution is quite naturally the recipient of many cases originating outside its walls,

but the mortality rate for a large city is large enough to show the serious character of the disease. Another interesting series of figures is presented by Dublin, based upon the records of a large life insurance company, in which it is shown that deaths from toxemias of pregnancy are only exceeded by those from "puerperal septicemia," and this was confirmed by comparison with the entire registration area of the United States for the years from 1910 to 1916.

The time at which the eclamptic seizure manifests itself varies within wide limits according to statistics presented by different writers. It is generally assumed that the intrapartum type is the most common, occurring in 46 per cent of the cases, according to Olshausen; and in 61 per cent, according to Knapp and Lichtenstein. Williams estimates that 55 per cent of the cases are found before labor during the latter months of pregnancy. McPherson, basing his estimate on the statistics of the New York Lying-in Hospital, states that about one-third of the cases occur postpartum. A similar divergence of opinion is found in regard to the prognosis. Many claim that the postpartum variety offers the worst prognosis, because the fetus and placenta as possible exciting factors have already been eliminated and yet the toxemia is evidently severe enough to produce an explosion. Undoubtedly the best results attend the cases coming on during labor, as delivery is usually accelerated by the seizures and the cervix properly prepared for a more rapid expulsion of the child. It is difficult in any case to estimate the outcome, as many women die with a history of only a single convulsion and others survive after a great number. I have had a personal experience with a case in which recovery took place after seventeen severe general convulsions lasting over a period of three days, the patient making a complete recovery with spontaneous delivery of a macerated, premature fetus about ten days after the beginning of the attack.

Clinical Course.—In a typical case of eclampsia the symptoms are so characteristic that they constitute a well-marked clinical picture which may be briefly described as follows: Premonitory symptoms including malaise, headaches, either frontal or occipital, puffiness of the hands, distinct edema of the ankles and lower abdomen, and visual disturbances, including spots before the eyes, blurred vision, and transitory attacks of blindness, often precede the attack by varying periods of time. Immediately before the

seizure we may note irregular abdominal pains, frequently localized in the epigastrium, nervousness, restlessness and other vague sensations, increased dizziness and visual disturbances.

In other cases, however, no premonitory symptoms have apparently been present, although close questioning, when recovery has set in, will often elicit the desired information. The premonitory symptoms noted may be followed by a sudden general convulsion, succeeded by a period of coma, or slight muscular twitching, involving the smaller muscles of the face and hands, may be observed by the patient herself, followed by a general tonic or clonic convulsion involving the larger muscular groups. The patient throws herself about on the bed, or may sink to the floor; the seizure is accompanied by a clinching and grinding of the jaws with consequent laceration of the tongue. Foaming at the mouth is usually present and the patient becomes markedly cyanotic. The convulsive movements then gradually cease and the patient sinks into a deep coma from which a complete recovery may result before the next convulsion comes on, or the convulsions may succeed each other very rapidly without any intervening period of lucidity. The interval between the convulsions varies. If sedatives are administered as well as other treatment, the seizures occur at intervals of several hours or sometimes of several days, but in the more violent cases rapidly succeeding convulsions without any intervening periods of consciousness may be followed by early fatal termination.

In the majority of cases the administration of sedatives has a marked effect in reducing the number and severity of the seizures, but in certain instances nothing seems to check them, not even the emptying of the uterus. When the convulsions subside a hemiplegia involving one or more muscular groups is sometimes noted as the patient comes out of the coma. If due to hemorrhage the paralysis remains a permanent one, or is very slowly recovered from, but if produced by a localized edema of the brain or by a very small clot, complete recovery rapidly follows.

In cases where the seizure comes on during the later months of pregnancy and the patient is not already in labor, it may come on very quickly and one is often surprised that primiparous patients with rigid, undilated cervices undergo rapid softening and dilatation of the latter with delivery within a period of several hours. I have observed in a number of instances spontaneous

labor during a slight attack; in other cases, as already noted, recovery from the convulsion may result and the patient may go on with her pregnancy to some later date with a spontaneous delivery of a dead child, or, in some instances, a living one. When the attack comes on during labor itself, rapid delivery usually occurs if no dystocia is present.

In Puerperium.—Eclampsia developing during the puerperium may manifest itself at different periods after delivery, sometimes within a few hours, and in some instances a diagnosis of eclampsia has been made when convulsions come on several weeks after delivery. We may assume, however, that in such cases the convulsions were due to another cause. Although postpartum eclampsia may manifest itself in the form of only one or two general seizures, cases are frequently reported in which the condition is extremely severe with early fatal outcome. In most of these cases we have no premonitory warning symptoms and the patient, apparently well, suddenly develops a general tonic or clonic convulsion most unexpectedly. The period of coma which succeeds the convulsion is followed by recovery in which the patient may have no recollection whatever of the convulsion itself, and is merely reminded by her lacerated tongue of the fact that something was wrong.

Without Convulsions.—Eclampsia without convulsions is now recognized as a distinct clinical entity, since Schmorl first made a report of three such cases in 1902. The absence of the characteristic convulsive seizures has frequently led to some other diagnosis, such as uremia. In these patients a gradually developing coma may or may not be preceded by the aura described in connection with the symptoms of an ordinary eclamptic seizure. Usually a rapidly developing coma is noted which may last for varying periods, or in which the patient may suddenly expire. Autopsy affords a key to the diagnosis and we then note the characteristic hemorrhagic and degenerative lesions associated with the better known types of the disease. In such patients we often find excessive hemorrhages into the lateral ventricles, or in the region of the pons, such as are described in the section on pathology, as having occurred in some of the cases at the New York Lying-in Hospital.

Peripheral Nerve Lesions.—In addition to the more or less permanent lesions of the central nervous system already noted as

complications of the eclamptic seizure, one may find transitory involvement of various peripheral nerve groups with characteristic pain, loss of function, etc. A so-called neuritis of this type may persist for many weeks after the patient recovers. In some cases permanent mental derangements have been noted with development of a psychosis which is often permanent. In every case of insanity developing during the puerperium the possibility of a toxemia should be borne in mind and the treatment directed towards this possibility. The instances of hemianopsia which have been noted after eclampsia are undoubtedly due to central cerebral lesions and must be distinguished from the permanent visual disturbances due to retinal hemorrhages and separations. Where an edema of the retina is present this usually disappears; but, if hemorrhages have occurred, particularly if they are associated with marked nephritis, recovery with restoration of normal vision may be considerably delayed. Should the optic nerve be involved a permanent damage to vision may result.

Blood-pressure.—Increased blood-pressure is generally regarded as an essential accompaniment of various toxemias of pregnancy, although Lynch, of San Francisco, and others have shown that eclampsia may occur without such elevation. Hypertension is accepted as a certain sign of toxemia, because arteriosclerosis is most uncommon during the child-bearing age. A constantly increasing number of cases has been reported, however, where high blood-pressures were not accompanied by evidences of toxemia. There does not seem to be any relation between the amount of albumin in the urine and the height of the pressure. Lynch reports two cases of eclampsia in which no premonitory symptoms were present; in the first of which the highest pressure was 113 during labor; in the second, 125. In the second case convulsions came on two hours after delivery. The urine in both cases was negative. In a third case of eclampsia there were no convulsions but a deep coma, the highest pressure reading being 100. This case was fatal. Lynch also refers in this article to other cases gathered from the literature.

F. C. Newell found normal variations from 100 to 130 in a series of 150 pregnant women. Only one patient within these limits developed eclampsia. He claims that if the pressure is over 130 the patient should be kept under close observation, even in

the absence of other symptoms. In this series about 11 per cent showed albumin. Newell believes that a temporary rise of blood-pressure may occur during pregnancy without the development of other symptoms.

In connection with elevations of blood-pressure, it is necessary to take into consideration the presence of other symptoms before making a prognosis. Edema of the legs, with high pressure, is always significant, and if the albumin is present, it is dangerous. Other observers have repeatedly confirmed these findings, so we may rely on their value as a prognostic indication.

While reasonable limits should be recognized for blood pressure readings, the individual patient must always be considered. A stout, vigorous, active, well-nourished woman may furnish readings of 140 to 150 (systolic) that need not cause any alarm if unaccompanied by other symptoms. These figures in a less vigorous patient, with possibly other attendant symptoms, should, on the contrary, be given due consideration. In some patients, blood pressure readings may be abnormally low, 90 to 110 systolic, and here we usually find other evidences of a general asthenia.

To avoid any possible extraneous factors in taking routine ante-partum blood pressures, the patient should be on the examining table in the prone position, with all constricting articles of clothing loosened. The mercury manometer is preferable to the spring instrument for office and bedside use and several readings should be taken. Personally I prefer the auscultatory method. In numerous instances I have seen the pressure drop 20 to 40 points after a patient had lain on the table for a few minutes and had her "nervousness" relieved by reassuring conversation. It is advisable in such cases to resort to means for elevating the pressure, and when this has reached higher figures (120 to 130), the patient will be found to be much more comfortable.

Significance of.—High blood-pressure resulting in an acute edema of the brain has been prominently identified with the etiology of eclamptic convulsions by Zangemeister. He insists that the early symptoms are those of pressure, and that the measures which have been successfully employed act by reducing the edema and the local irritation. Labor pains raise the blood-pressure and increase the cerebral edema, according to Zangemeister, but venesection lowers the pressure and therefore reduces the convulsions. This author even goes so far as to advise

osteoplastic resection of the skull in severe instances and has actually performed the operation in several instances to which more detailed reference will be found in the section on treatment.

Urine in Eclamptic Seizure.—An examination of the urine obtained during or just before an eclamptic seizure shows that it contains high percentages of albumin, and in most cases boils solid. Hyaline, granular and often blood casts are present. The

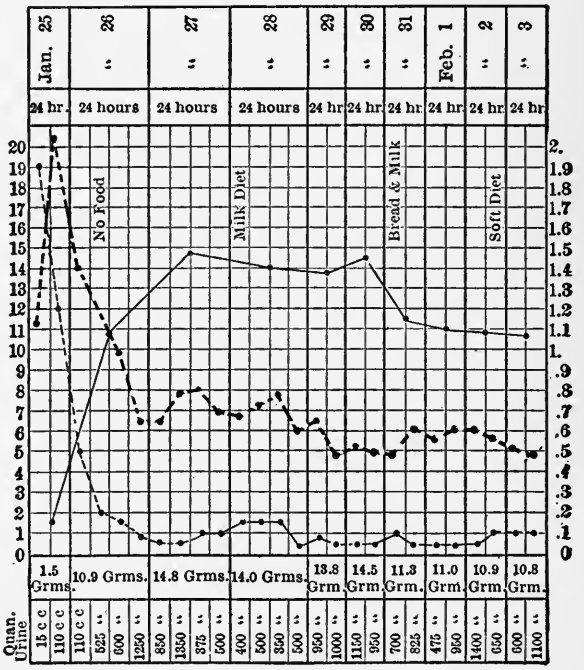

FIG. 5.—URINARY CHART FROM A CASE OF ECLAMPSIA WITH RECOVERY, SHOWING THE TOTAL NITROGEN AMMONIA AND ALBUMIN. The figures on the right side indicate the percentage of albumin and on the left side the grams of total nitrogen and percentage of ammonia nitrogen. The total nitrogen is shown by the solid black line, the ammonia by the heavy dotted line, the albumin by the lower, more lightly dotted, line (Williams).

specific gravity is high and the acidity marked. With the subsidence of the seizures and the recovery of the patient, the albumin rapidly disappears; this offers a good prognosis for the individual case (Fig. 5). The finding of large quantities of albumin even before convulsions is not unusual and I have personally observed cases in which daily specimens of urine boiled practically solid and yet no actual convulsive seizures resulted. There are other urinary changes, including a marked reduction in the amount of

nitrogen and its derivatives, while creatinin, amino-acids, and similar bodies are relatively increased because the total amount of urine is markedly diminished. Further details of the urinary findings in eclampsia are included in the chapter devoted to the subject.

Rôle of Kidneys.—It is necessary, however, in considering the etiology, to refer to the urinary organs themselves as possible factors in the production of eclampsia. Improper kidney function was long considered one of the principal causes of eclampsia, and it is quite natural that many of the investigations should have been directed to this source. Moreover, autopsies show that in most cases the kidneys present undoubted evidences of lesions. Whether the kidney lesion may be regarded as the primary disturbance and the toxemia a secondary phenomenon, or whether the reverse is the case, is a matter that is still undecided. Many authors insist that the kidney disturbance is the primary trouble and that the organ is either already the subject of an inflammatory or irritant process, or that its aberrations are due to disturbances in the circulation from mechanical causes. Pressure on the kidney or its excretory tube by the growing uterus is believed to be the sole cause by some authors, who consider this finding sufficient to recommend the emptying of the uterus as the logical thing in the treatment in order to relieve both traction and compression. When the kidney yields readily to the displacing force, the circulation is not disturbed, but, if the capsule is thick or the kidney is not freely movable, its blood supply is interfered with. We may also allude here to the assertions of Edebohls and his followers that the only relief in eclampsia can be secured by operative stripping back of the kidney capsule in order to permit the restoration of its circulatory conditions.

Frequency of Renal Infection.—The frequency of renal infection in pregnancy, according to Bugbee, is not generally appreciated. Although this writer believes that the process is hematogenous in a large percentage of cases, and that it originates in the colon, an important element is lowered resistance, or interference with drainage due to pressure on the ureter from the enlarging uterus, particularly on the right side, or torsion, stretching and kinking of the tube. Whether the development of this bacteria has anything to do with the production of eclampsia or a predisposition to it, or pregnancy nephritis, is still an un-

solved problem, but the elimination of toxic material due to intestinal putrefaction through the kidneys must be borne in mind. The necessity of improving the drainage from the colon by appropriate measures is thus evident. This would mean a corresponding diminution in the number of bacteria passing through the kidneys and of their influence on these organs.

Infections other than Renal.—Infection of other than renal origin has often been cited as an important factor in the production of eclampsia. Stroganoff advocated this theory for the following reasons: Eclampsia is a general disease affecting all parenchymatous organs; it resembles an acute infection by beginning explosively or after a prodromal stage; it is accompanied by fever; one attack confers immunity (?); it seems to have an epidemic form. In support of his views Stroganoff describes 126 cases (10 occurring in the early months of pregnancy), in which, after the cessation of the eclamptic seizures, the pregnancy continued to a normal termination. La Vake later took up another aspect of the subject. He refers to the view of Young of Edinburgh, more fully discussed on a later page, that pregnancy toxemia is due primarily to placental infarcts caused by thrombosis of the uterine vessels, and holds, furthermore, that the cause of the thrombosis of the vessels is an infection from some primary focus. La Vake draws a parallel between nephritis following a chronic septic condition and that occurring during pregnancy, and attempts to emphasize the resemblance by citing 13 case reports in which evidences of an infectious condition were apparently present.

Dental Foci of Infection.—No attempt has been made to isolate a specific organism in explaining the possibly infectious character of eclampsia, but various sources for the development of such a process have been described. Among others we find an interesting suggestion by J. E. Talbot, who insists that the fundamental cause of eclampsia is not to be sought in the products of conception. Prompted by the findings revealed by X-ray examinations of the teeth in one of his cases of eclampsia, Talbot subjected a series of 97 cases of toxemia to the X-ray, and claims to have found evidence of chronic sepsis in the teeth in all without a single exception. The fact that in many cases there is evidence of activity in dental pus pockets just preceding the occurrence of toxemia, or complicating it, and the fact that the severity

of the symptoms is not generally proportional to the amount of chronic sepsis present, are evidences which tend to show that there is a relationship between chronic sepsis and the incidence of the disease.

That the presence of a chronic septic process has a secondary effect on the kidneys is well known. The toxins of acute infection produce an inflammatory reaction in the kidneys with an inhibition of their excretory functions. This reduces normal elimination. Talbot, therefore, considers it a reasonable hypothesis to assume that the symptoms of the toxemia of pregnancy are caused by the retention of the normal physiological waste products of the developing pregnancy, this retention being due to the damaged functional power of the kidneys, which damage has been brought about by the toxins of chronic sepsis in the blood. A vicious circle is thus established. The toxins of chronic sepsis, by their inhibition of the kidney function, cause a retention of the normal waste products of the body. These waste products are also injurious to the excretory function of the kidneys when they are present in abnormal concentration in the blood. Nature's endeavor to improve this situation is reflected in the rise in blood-pressure, and this is now accepted as the earliest evidence of the presence of toxemia. Many cases are on record in dental literature, as well as in medical writings, which demonstrate the good results obtained in cases of arterial hypertension by removal of foci of infection from the teeth. It has also been reported that certain cases of albuminuria have been cured by the same means.

The pathological findings in the liver and placenta may also be explained by the same theory of septic infection, these local lesions being due to the presence of infarcts. The presence of the latter as a cause of placental separation is admitted.

Early Autolysis of Placenta.—The reference in a previous paragraph to the views of J. Young, of Edinburgh, on the relationship of eclampsia and accidental hemorrhage, calls for more extended comment. As the result of a very complete anatomical experimental investigation at the Royal College of Physicians Laboratory in Edinburgh, Young summarized his work by the statement that eclampsia and the albuminuria of pregnancy are due to the liberation of the products of early autolysis of the placenta. He has attempted to establish this theory by the fol-

lowing considerations: (1) The toxemias are especially associated with recent infarction of the placenta. In severe cases ending rapidly in labor there may be no visible evidence of placental disease, but if the placenta is born several days after the attack, massive necrosis may be seen. (2) Placental infarction is due to an interference with the maternal blood supply of the part. He believes that it can be shown conclusively that the chorionic elements are dependent upon the maternal blood supply and can live so long as this is retained, even if there is no fetal supply. (3) Interference with the blood supply, which was responsible for the infarction, is not dependent upon a toxic state and may occur in the most extreme form where there is no evidence of a toxemia, for example, accidental hemorrhage. (4) The placenta is so constructed that, if part of it die, the products liberated from the dying patch can pass directly into the blood stream (Figs. 6, 7, 8, 9). In order, therefore, to establish a toxemia a circulation of blood surrounding the poison-generating foci is necessary. This explains the cessation of symptoms with the death of the child and separation of the placenta, and also explains the absence of toxemia in cases of accidental hemorrhage in which the placenta is completely detached by the blood clot or by other means. The cases of accidental hemorrhage associated with a toxemia are those in which part of the placenta remains attached for some time. The necrosis in this part liberates toxic materials. (5) Where the placental disease is gradual in its onset there is more chance of the evolution of the infarcted patches. This explains why in long-standing albuminurias there may be more visible placental disease than in acute eclampsia. (6) These facts all suggest that the toxemias are due to the autolytic products liberated in the early stages of the placental death. By imitating this process which occurs *in utero* it has been possible to isolate from the healthy placenta a soluble material which reproduces the clinical features and morbid changes which are especially characteristic of eclampsia, including convulsions, peripheral focal necrosis in the liver, and degenerative lesions in the kidney, especially located in the convoluted tubules. Young admits, however, that the occurrence of post-partum eclampsia stands in the way of a complete adoption of his theory. He believes that the evidence is of sufficient importance to warrant in all such cases

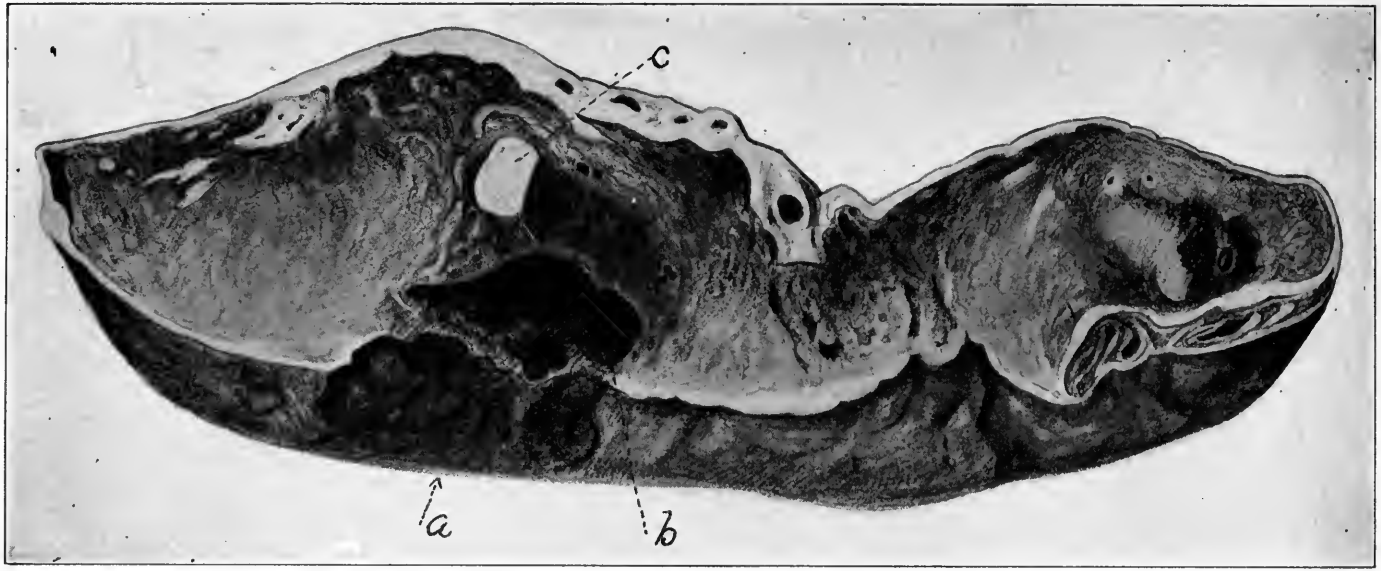

FIG. 6.—SECTION OF THE PLACENTA FROM A CASE OF ALBUMINURIA. Shows recent retroplacental clot (*a*); subtended accurately by a recent infarction which is marked off from the surrounding placenta by its darker color; (*b*) the disappearance of the hemoglobin in the blood cells has resulted in the production of a pale infarct. (*c*) This and the three following cuts are adapted from Young's paper, in the Proc. Roy. Soc. Med.

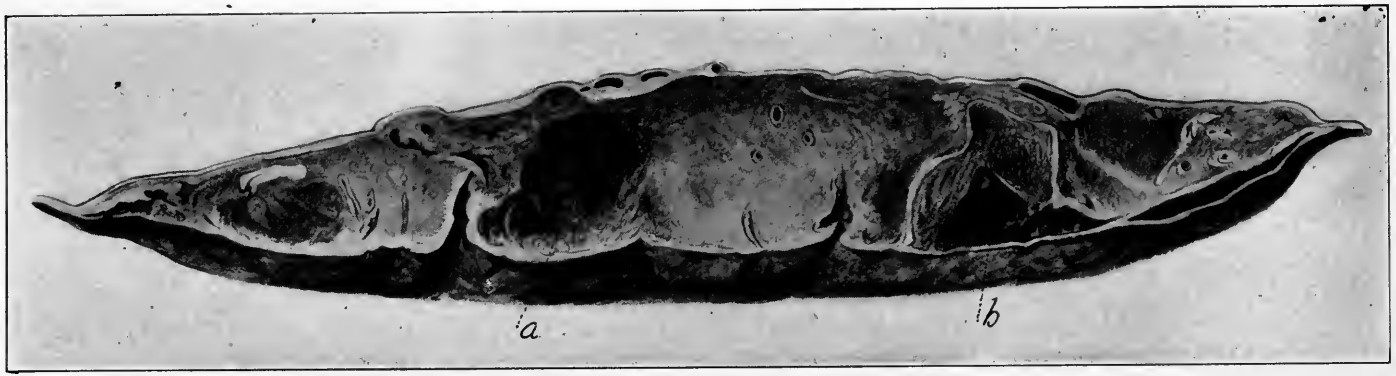

FIG. 7.—SECTION OF A PLACENTA FROM A CASE OF ECLAMPSIA SHOWING TWO STAGES IN THE INFARCTION PROCESS. The more recent (*a*) shows no evidence of its origin; the old one (*b*) surmounts a retroplacental clot and shows by its paler color, especially at the periphery, the solution of hemoglobin. During this time the toxic products of necrosis have diffused with the blood which circulates around about in the healthy placenta (Young).

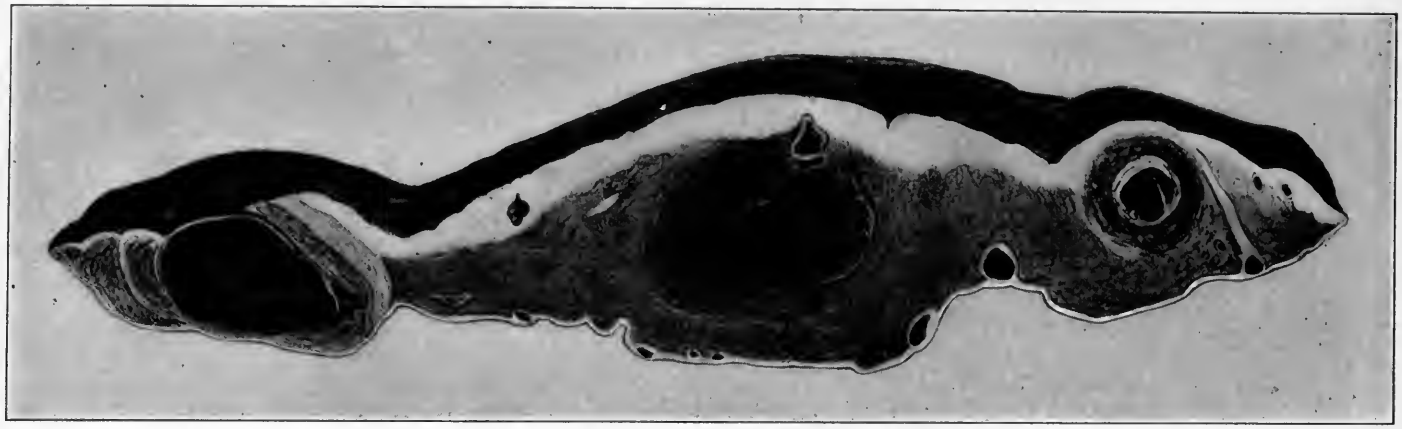

FIG. 8.—SECTION OF PLACENTA FROM A CASE OF SEVERE ALBUMINURIA, SHOWING RETROPLACENTAL AND INTRAPACENTAL HEMORRHAGES IMBEDDED IN AND SURROUNDED BY HEALTHY PLACENTA. The relation of the infarcts to the clots indicates that the necrosis is due to the interference with the maternal blood supply consequent upon the hemorrhage (Young).

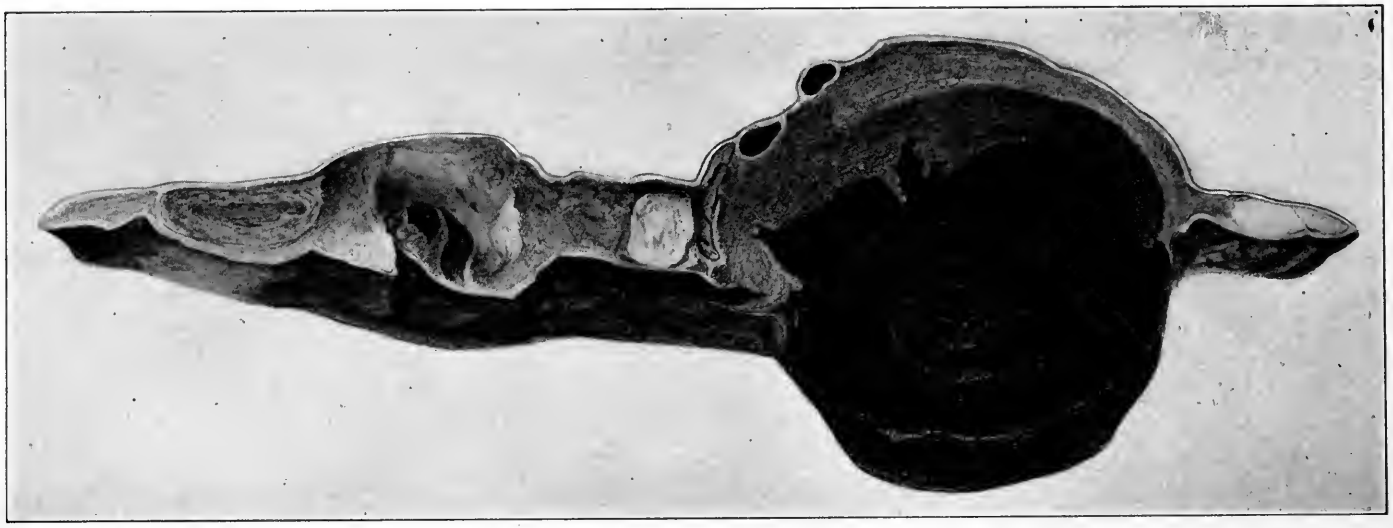

FIG. 9.—SECTION OF PLACENTA FROM A CASE OF ACUTE TOXEMIA, SHOWING LARGE RETROPLACENTAL CLOT (ACCIDENTAL HEMORRHAGE) SUBTENDED ACCURATELY BY A RECENT INFARCT. This is formed as the result of the interference with the maternal blood supply. To one side there is a smaller, old infarct and another of recent formation (Young).

a thorough exploration of the uterus for a possible piece of retained placenta.

Internal Gland Function.—The association between eclampsia and disturbed internal gland function has been made the subject of many studies, and a wealth of bibliographical references show how much in favor these speculations have been with students of the subject. The readily observed changes in the thyroid gland in pregnancy led long ago to the thought of its possible participation. Thus it has been assumed that the failure of the thyroid gland to become hypertrophied during pregnancy is probably followed by insufficient metabolism and may result in various forms of toxemia of pregnancy. Graves' disease, by materially altering the quantity and quality of the thyroid secretion, is believed to have an important influence upon metabolic processes; therefore, if associated with pregnancy, owing to the increased metabolism incident to that period, it becomes a grave complication.

Opotherapy.—When there is a failure of the normal hypertrophy of the thyroid during pregnancy, or when there is a diseased thyroid (as in Graves' disease), the administration of thyroid substance, by supplying the deficiency of the normal thyroid secretion and by diuretic action, has been claimed to improve a faulty metabolism and thus have a favorable influence upon the manifestations of the toxemias of pregnancy. George Gray Ward, Jr., found in two cases that the use of a saline extract of thyroid proteins made from fresh normal human glands is more efficient in rapidity and reliability of action than the ordinary sheep thyroid extract. The hypodermic administration is superior to oral use, especially in cases of toxic vomiting or eclampsia. In a subsequent paper Ward claims that, when there is a high ammonia output, as shown by the nitrogen partition, thyroid administration is indicated. Ward finally concludes that it is necessary to distinguish two types of toxemia: (1) Those cases with no Graves' disease, but without sufficient thyroid secretion to promote the increased metabolism in the liver made necessary by the pregnancy, and probably due to the failure of the thyroid to become hypertrophied. (2) Cases associated with Graves' disease, which condition usually causes serious disturbance in the metabolism.

Exophthalmic Goiter in Pregnancy.—A. Crotti, in an extended review of the subject of goiter and pregnancy, states that the coin-

cidence of pregnancy with exophthalmic goiter is unusual, and the observation has been made that it is much rarer in hospital than in private practice. In the Seitz collection of 112 cases of exophthalmic goiter there was apparently no change in about 40 per cent of the cases, and he states that a small number even showed some improvement during pregnancy. On the other hand, 60 per cent were made distinctly worse by gestation. In about one fourth of these cases, the thyrotoxicosis was a serious menace to life and health; seven patients died. In five cases therapeutic abortion was performed and in 11 cases premature labors occurred, with three miscarriages and three macerated fetuses. He includes seven cases in which thyroidectomy was performed during pregnancy. Theilhaber also found that the majority of cases of pregnancy coincident with Graves' disease were made distinctly worse, and the same conclusion was reached by Kleinwächter and Hirst. The latter even claims that this disease may have its origin in gestation, that it predisposes to uterine hemorrhage and may result in the death of the fetus. J. Whitridge Williams believes that pregnancy exerts a deleterious influence on Graves' disease and that the tachycardia is greatly increased during this period. Crotti declares that women with exophthalmic goiter should not marry, and if they marry, pregnancy should be avoided.

Effect of Thyroidectomy on Pregnancy.—I have had an opportunity to observe a pregnancy in a patient in whom thyroidectomy had been performed. This patient, age thirty-two, primipara, gave a history of thyroid enlargement for which an operation was performed about one year previous to her pregnancy. The latter was characterized by continued attacks of nausea and vomiting, extreme nervousness, flushes and tachycardia. The urine was normal except for a high specific gravity. In the belief that some of the symptoms might be due to the lack of thyroid secretion, thyroid extract was given in small doses continuously but no effect was noted. A moderate degree of hydramnios developed in the latter months and the patient's condition became very uncomfortable. Towards the end of the calculated term of pregnancy evidences of kidney disturbance appeared, including marked traces of albumin, granular and hyaline casts. Attempts at induction of labor were not very successful and finally abdominal cesarean section was performed under gas, oxygen and ether

anesthesia. The extraperitoneal procedure was followed in view of the prolonged labor, the frequent examinations and the presence of a temperature of 102° F. As the uterus was being incised it was found to be in a state of tonic contraction, aggravated, no doubt, by the administration of 0.5 cubic centimeter of pituitrin before the abdomen was opened, and without the knowledge of the operator. The extraction of the fetus was rendered very difficult and a stillbirth resulted. Some sloughing of the fascial layer of the abdominal wound subsequently occurred, but as soon as this separated prompt healing resulted. During convalescence the headaches disappeared, the urine increased in amount, and the general condition improved. Three weeks later an exacerbation of the nephritis occurred.

In a subsequent discussion of the above case at a meeting of the New York Academy of Medicine, Dr. Harold C. Bailey remarked that possibly a condition of hyperthyroidism rather than hypothyroidism was present, as hyperthyroidism had been known to persist as long as eighteen months after the removal of the gland. Another speaker, however, believed that the symptoms should be ascribed to hypothyroidism and, although the surgeon's report stated that sufficient thyroid tissue had been left behind, this was probably only sufficient for normal metabolic processes. As the thyroid during pregnancy must compensate for ovarian hypofunction its glandular activity was insufficient and therefore was a contributing factor to the patient's toxemia.

Pertinent to the subject is a comparatively recent clinical study by L. F. Watson based on severe cases of toxic goiter with exophthalmos and 9 cases of toxic non-exophthalmic goiter occurring during pregnancy. It is probable that patients with goiter of a brief duration ascribe their increase in symptoms to the pregnancy itself, while in reality the symptoms are due to a beginning hyperthyroidism. In cases of pregnancy, when the exophthalmic goiter is accompanied by symptoms, an operation is attended by more danger than in the nonpregnant patient, and is not considered advisable unless the goiter causes serious difficulty in breathing. Watson states that he secured good results with quinin and urea injections made directly into the gland in order to produce localized aseptic necrosis of a portion of the hyperplastic thyroid. He believes his procedure is without danger to mother and child.

In cases associated with deficient thyroid function and kidney disturbance, thyroid may be administered continuously throughout the gestation and should not be stopped until delivery is completed. In the presence of hyperthyroidism the danger of convulsions is increased and they may appear without the presence of albumin or casts. In such cases cesarean section affords the best chance for the patient, although Gellhorn advocates vaginal section under spinal anesthesia. Induction of labor is contra-indicated because of its slowness.

Thyroid and Parathyroid Opotherapy.—Notwithstanding the claims for therapeutic success with the administration of thyroid gland in eclampsia, which are based on the apparent connection between abnormalities of the thyroid secretion and the production of eclampsia, there is no definite proof of the thyroid origin of this disease. The lack of proof in this direction has called attention to the parathyroids and their inadequate functioning which has been assumed to be a cause of eclampsia. Thus Massaglia states that the parathyroid theory of eclampsia and its treatment by this gland have long been advocated, especially by Italian writers. He reports experiments made on two dogs from which he removed the parathyroid when they were ten weeks old. Both animals grew up apparently healthy except for traces of albumin in the urine. When they became gravid they seemed to thrive for about two months and then each in turn developed severe tetany. The author regards this experimental tetany as the equivalent of eclampsia in women and emphasizes the fact that the tetany subsided under parathyroid treatment. In both of the animals the parathyroid insufficiency evidently remained latent until roused by the stress of the pregnancy to active manifestations. In the two experimental animals subsequent pregnancies showed a similar tendency to tetany, although less marked than at first. This also responded to treatment and was never apparent at any other time.

The Mammary Gland Theory.—Persistent activity of the mammary glands has been assumed to be a cause of eclampsia with such conviction that certain very radical measures of treatment are based upon the theory. Sellheim and other German writers even suggest the complete ablation of the breasts in such cases. This theory has its foundation in the astonishing clinical and pathological similarity between eclampsia and the so-called

parturient paresis or milk fever in cattle. This disease has long been recognized in veterinary practice in the Scandinavian countries and also in France. The apparent connection between the two disorders both clinically and pathologically has long been admitted. The recent work of Healy and Kastle has again called attention to the subject. A very complete contribution to the literature of the mammary gland theory has also been made by Wilson.

Experimental Confirmation of.—From experiments made in cattle, Healy and Kastle are of the opinion that eclampsia is due to a toxin similar to that of milk fever in cattle and elaborated by the breast in a similar manner. They believe that the toxin of this disease is developed in the udder as the result of its metabolism preceding normal milk production. The intense physiologic activity which is suddenly awakened in the mammary glands may easily be conceived to give rise to a great variety of disintegration products of varied chemical character which may be absorbed into the circulation precisely as milk sugar is known to return into the organism in this way at the beginning of lactation. They tested their hypothesis by experiments with the colostrum, and found that the first colostrum obtained from cows during an attack of parturient paresis had severe toxic effects when injected into other animals in contrast to the relative inertness of fresh milk or colostrum from normal cows. The post-mortem and microscopical examinations of the organs of guinea-pigs killed after these injections were presented to show the same pathologic degeneration and changes as are characteristic of eclampsia. The authors applied this theory with great success to the therapy of parturient paresis. The udder is subjected to acute dilatation by means of oxygen or sterile air, thus preventing by pressure the absorption of toxins and shutting off the blood supply of the milk glands until it has the opportunity to resume its ordinary excretory activity, and thus keeping the harmful products out of the blood stream.

Criticism of Theory.—We find, however, that parturient paresis occurs almost entirely post partum, while eclampsia shows no special predilection for this period. Parturient paresis increases in frequency in direct ratio with increased power in milk production while no such finding has been noted in eclampsia. Sugar is an almost constant ingredient of the urine of parturient paresis, but

is rarely found in eclamptic urine. It is evident, therefore, that further study should include a careful pathological and clinical examination of parturient paresis as well as a determination of the toxic or nontoxic character of the colostrum from eclamptics. A tentative trial should be made in properly selected cases of eclampsia by the treatment of air or oxygen injection in the breasts. Wilson, in his review of the subject, collected 29 cases of eclampsia in which attempts were made with varied success to limit absorption from the breasts in this manner.

However skeptical one may be regarding the mammary theory of eclampsia, the hypothesis, as pointed out by Wilson in his excellent review, is at least sufficiently plausible theoretically to be entitled to respectful consideration. Most textbook authors, however, dismiss the subject with scant courtesy, but we may yet be surprised by the results of closer attention to metabolism in the breasts as etiological factors in the production of eclampsia.

Abstraction of Calcium Salts.—The abstraction of calcium salts from the mother by the fetus as a cause of eclampsia has been brought forward by J. G. Drennan and others. It is generally believed that a certain amount of fatty infiltration of the liver cells around the hepatic veins is a physiological condition during pregnancy and lactation. Drennan disagrees with this view. He considers that this fatty infiltration is a pathological state due to the abstraction of calcium salts from the mother's blood by the fetus in such quantity as to deprive the mother of what is required to unite with the fatty matter in her liver cells to form lipoids or soluble fats. These fats would then be conveyed by her circulation to be deposited in tissues normally the dépôts of free fat or kept as a source of fat to the fetus. This fatty infiltration causes disturbed liver function with the production of toxins from imperfect protein digestion and the liver is thus unable to function. The prevention and treatment of this condition, therefore, consists in a liberal calcium diet and lessened protein food.

Intermediary Products.—Oliver, taking up this question from another standpoint, states that the eclamptic intoxication results from the intermediary products of nitrogen metabolism, and not from its end products. It is also due to the retention of these intermediary products in the nerve and muscle cells, because there is an insufficiency of the requisite mineral substances circulating in the body of the mother to satisfy her own needs and

those of the fetus. The demands made by the embryonic tissues for phosphorus and calcium exceed greatly that of the adult, consequently if there is an insufficient amount of these mineral substances in the circulating blood of the mother, the latter must suffer. The oxidation of the projected matter in the organism takes place in intimate union with the phosphorus in the living cell. If, therefore, from any cause the phosphorus content of the maternal tissues, especially that of the nerve and muscle cells, becomes lowered, then the formation of urea is hampered and the intermediary products of nitrogen metabolism accumulates in the nerve and muscle cells. Independent of the auto-intoxication which thus results, the relative ratios of the mineral substances in the maternal cells become so altered that the normal nerve and muscular reactions and irritabilities have changed and convulsions are readily induced. Oliver claims that the varied diet of to-day is very deficient in phosphorus and calcium. In the cereal grains there is an abundant supply, but in the white flour usually employed there is little or no phosphorus or lime. He thinks that a prophylaxis against eclampsia demands that the pregnant woman's diet should contain an abundant supply of the mineral substances.

Anaphylactic Reaction.—There is another field of considerable speculative interest in the study of the etiology of the disease which deals with the possibility of eclampsia as an anaphylactic reaction. Rosenau and Anderson first suggested this idea, which was afterwards elaborated by several German authors. The latter made a series of extensive animal experiments from the results of which they concluded that the mother undergoes a process of sensitization during pregnancy through the continuous absorption of small quantities of fetal protein material. Vertes endeavored to show by experiments that animals can be sensitized by their own albumin and that the symptoms of hypersensitiveness are practically identical with those of eclampsia. Vertes also stated that the organs of the animals presented the same changes post mortem as are found in organs of patients who have died of eclampsia. He draws the conclusions that eclampsia is merely a manifestation of anaphylactic shock due to the absorption of chorionic villi, and that the albuminuria of pregnancy is not merely a mechanical disturbance of function, nor a chemical

disorder caused by the excretion of the products of fetal metabolism, but is a premonitory stage of eclampsia.

Parenteral Introduction of Complex Protein. — Another theory along similar lines is advanced by Hull and Rhodenburg, who claim that with the exception of provocative injection and bacterial disease, pregnancy is the only condition in which complex protein material is introduced into the general circulation parenterally. Ferment-active homologous protein when introduced into the circulation induces extensive degeneration of the liver, but as a rule only slight degeneration in the kidney. The authors consider that these lesions in the rabbit are equivalent to those seen in the organs of eclamptic human females. They used homologous protein which had been previously boiled in order to destroy the enzymes. Slight lesions in the liver resulted, but the kidney was found damaged to a more marked degree. Large quantities of albumin and all varieties of casts were found in the urine. The animals died in convulsions and coma, reproducing the picture of eclampsia in the human.

Leucin.—Leucin as a product of autolysis produces after injection a marked degeneration of the liver both in rats and rabbits. Hull and Rohdenburg believe that eclampsia is developed in the following manner: An overload of fetal elements is thrown into the circulation, where it is autolyzed with the formation of an excess of leucin. This leucin injures the hepatic vessels with consequent thrombosis, cloudy swelling, necrosis and more or less complete autolysis added perhaps also to protein fractions incompletely broken down by the liver.

Dissenting Views on Sensitization.—The sensitization of the mother against fetal proteins has, however, been widely combated, especially in experimental studies made by Johnstone and others. Falls and Bartlett confirm the observation that proteins prepared from the placenta, when introduced under the skin, usually cause a local reaction in both pregnant and nonpregnant individuals. They believe that this reaction is not sufficiently well marked for diagnosis, and that it speaks against the theory that the pregnant woman is specifically sensitized to placental proteins. The lack of a general anaphylactic reaction in such cases likewise supports this view. Eisenreich also tried to show experimentally, by means of the passive transmission of hypersensitiveness, that eclampsia is not an anaphylactic phenomenon.

He sensitized several guinea-pigs by intraperitoneal injections of maternal serum, and after from twenty-four to thirty-six hours he gave an intravenous re-injection of fetal serum. Among 50 guinea-pigs thus treated, 41 showed no symptoms, while the others showed the noncharacteristic pseudo-anaphylactic symptoms. Guinea-pigs treated with the serum of eclamptic mothers or their children failed to show any reaction and not a single animal died from shock. This observation seems to contradict the theory that eclampsia is an anaphylactic phenomenon. Eisenreich also attempted to demonstrate the fact that the complements in normal and eclamptic pregnant women do not support the assumption that there are any anaphylactic relations between mother and child. But the complement experiments showed clearly that in eclamptic patients biological processes are taking place that do not occur in the normal pregnant woman. The complement content of the serum of a normal pregnant woman is practically constant, while that of the eclamptic woman shows great variations, although not uniform ones.

Liepmann, who has also studied the relation between anaphylaxis and eclampsia, claims that eclampsia usually attacks robust, well-nourished women, whereas the weak and nervous type are affected by anaphylaxis. Edema and albuminuria are present in the former while exanthema with fever are noted in the latter. He claims that if eclampsia were caused by an ingress of foreign albumin into the maternal blood from the placenta, then, with each succeeding pregnancy, the body would become more and more sensitive; that is, eclampsia would become more frequent in multiparæ than primiparæ. Observation shows that the reverse is true, and the author therefore concludes that the albumin of the placenta which passes into the maternal stream in every pregnancy is not foreign albumin. Eclampsia and anaphylaxis have, therefore, nothing in common, according to Liepmann.

Prognosis for Fetus.—A final thought in discussing the subject of toxemia must be given to the fetus. The prognosis for the fetus in eclampsia is bad, because of the asphyxia produced during the convulsions, especially in a premature infant. Even if born alive and not incapacitated by a lack of development, convulsions are not unusual during the first twenty-four hours and are often fatal. But the fate of the fetus in the presence of other varieties

of toxemia must also be considered. Hertwig in his textbook on embryology suggests that the formation of monsters may be due to the presence in the blood of the mother of certain toxic substances, including alcohol. He bases this opinion on experiments in which the developing egg in lower forms of animal life underwent deviations from the normal when subjected to the external influences of various poisonous substances. These changes were independent of those produced by traumata. Werber reported an interesting series of experiments made on certain fish eggs subjected to the influence of oxybutyric acid and acetone. He found that a variety of defects in essential organs were produced, and we may reason by analogy that as these compounds are known to result from faulty metabolism in a pregnant woman a similar effect may be produced on the unborn child. No further evidence has been adduced, but it is well known that abortions and premature deliveries may result from the presence of a diseased endometrium or an improperly functioning placenta. Although the theoretical possibility exists, it seems to be contradicted by the practical findings in many cases of eclampsia in which the child at birth is free from defects in development, although it later presents certain evidences of toxemia which may result fatally. The subject is one deserving of more attention, and it is possible that further research along these lines may explain certain common monstrosities, such as hydrocephalus, congenital dystrophy, etc.

Errors of Metabolism.—The foregoing pages present by no means all the theories advanced to explain the etiology of eclampsia, which has been aptly termed the disease of theories. We have no definite proof that any one of the causes mentioned, or any group of them, are at fault. We simply know that a profound intoxication is present, but whether from maternal or fetal sources is yet undetermined. For want of a better term, "errors of metabolism," offers a suitable designation, and we seem every day to gather more facts to substantiate in a general way, the assumption that such "errors" constitute at least one of the leading factors in the production of the disease.

Influence of War Diet.—Interest therefore attaches to observations made during the late war on the incidence of eclampsia by Warnekros and other German writers who noted reductions in the number of cases of eclampsia in various clinics during this

period. Mayer attributed the change to the reduction in the frequency of sexual contact, for he considers the repeated introduction of spermatozoa in the female organism as a factor in producing anaphylactic processes. But this theory is regarded as farfetched by his German colleagues, who attribute the lessened occurrence of eclampsia to the lowered protein and fat contents of the war diet, which brought about a reduction in the functional hyperactivity of the liver and kidneys so often found in the second half of pregnancy.

These observations on war diet reduction seem to be in agreement with those made by others in peace times, for it has often been stated that eclampsia is more frequent in northern than in southern countries and that strong, full-blooded women are more frequently affected than those who are thin and less well-nourished. The geographical differences are attributed to variations in the diet—a greater amount of fat being taken in the northern and more vegetables in the southern, latitudes. A French observer, Lafont, has noted that in Algiers the wives of the natives are much less frequently afflicted with eclampsia than the wives of immigrants, which he explains by the fact that the natives eat more vegetables and the immigrants more salty foods. In Turkey eclampsia is stated to occur rarely and in one of the largest lying-in hospitals of Constantinople an average of only two cases a year has been observed. It has also frequently been claimed that eclampsia is more frequent during the winter than the summer months, which may be assumed to be due to the influence of the food, as more fat is taken in the colder season than during the warmer period.

Variations in Diet.—It is to be expected that the clinical picture usually recognized as pregnancy nephritis, which is frequently a forerunner of eclampsia itself, can be favorably influenced through changes in food stuffs. For instance, Warnekros' report from Bumm's Clinic in Berlin, shows that the incidence of nephritis during the two war years of 1915 and 1916, was about 1 per cent of the total number of labors, while during the four previous years it had varied from 2 to 4 per cent. These figures were confirmed by an examination of the statistics of three other large obstetric hospitals in Berlin. The number of eclamptic cases showed a similar diminution, being 1 per cent or less, in each case as compared with from 2 to 4 per cent during the years

before the war. Warnekros thinks that these observations indicate that there is a marked relation between eclampsia and diet, and, therefore, point the way to the prophylactic treatment of the disorder.

Epilepsy and Eclampsia, Differentiation of.—Before concluding the description of the etiology and symptomatology of eclampsia it is important to note at this point some other conditions in which convulsive attacks occur. Thus, it is essential to distinguish between epilepsy and eclampsia, for the beginning of epilepsy during pregnancy is serious in the sense of a possible later recurrence or persistence of the disease, while eclampsia, if recovery ensues, means restoration to health in most cases. On the other hand, a single epileptic seizure is of little consequence, while an eclamptic attack is much more serious and dangerous. The points in the differential diagnosis between these two conditions may be summarized as follows: The history of a previous seizure is usually to be noted in epilepsy at other times than during the period of gestation, the recovery without coma is rapid, there are no urinary signs of toxemia, the seizures extend over prolonged periods and do not recur at brief intervals as in eclampsia, and no pathological organic changes occur.

Binswanger and others have pointed out the increased disposition to recurrence of epilepsy during pregnancy in women who had seemed free from the disease for many years. This fact must be borne in mind in those cases where convulsions occur in succeeding pregnancies. Positive urinary findings with respect to albumin and casts are often necessary in doubtful cases before a definite diagnosis can be made.

Uremia and Eclampsia, Differentiation of.—The presence of uremia in the ordinarily accepted sense during pregnancy must also be taken into consideration in those cases where coma without convulsions constitutes the clinical picture. In certain cases convulsions may appear at varying periods after the beginning of the comatose state. The differential diagnosis must often depend on the knowledge of a previously existing chronic interstitial or glomerular nephritis combined with a reduced excretion of urine. As the treatment is practically the same, the question of immediate differential diagnosis need not be taken into consideration, although in a true uremia the prognosis is necessarily bad.

Chorea and Eclampsia, Differentiation of.—The occurrence of muscular spasm due to chorea frequently demands differentiation from such symptoms due to a toxic cause. The increasing frequency of this disturbance, as noted in medical literature, merits further attention. Chorea formerly was regarded in the same category as hyperemesis; that is to say, as a purely nervous disturbance occurring during pregnancy. It is well known that a previous history of chorea is found in most cases that present this symptom during pregnancy; but it is also an acknowledged fact that the convulsive seizures characteristic of chorea may become very much aggravated during this period, and if they are of a general, rather than a local, type, may even become confused with true eclampsia. Experience has shown that we must consider severe cases of chorea in pregnancy as a separate entity, perhaps of a toxic character. We often find associated with it other evidences of a toxemia, such as albuminuria, headache, slight degrees of jaundice, high blood-pressure, etc., so that it may be quite difficult to draw a line of distinction between chorea and toxemia as we ordinarily know it.

Mortality of Chorea in Pregnancy.—The mortality of the severer cases of chorea is rather high, being estimated by various observers as ranging from 17 to 30 per cent. In severe cases, the progress is very rapid toward a fatal issue unless the pregnancy is interrupted. In many of these cases, where the women have had several children, the history of progressively worse attacks will be noted in successive pregnancies, and the ordinary methods of treating chorea, including the administration of arsenic, iron, or the salicylates, seem practically useless. Autopsies performed in fatal cases of chorea have shown practically the same severe degenerative processes in the liver and kidneys as in eclampsia, although this is denied by some writers. Thus, Liepmann speaks of a personal case in which he noted cerebral hyperemia with thrombosis of the longitudinal sinus, edema of the dura, emboli in the large and small veins, areas of softening in the cord and degenerative processes in the ganglion cells of the central nervous system as well as of the peripheral nerves.

Symptoms of Chorea in Pregnancy.—In severe cases of chorea the convulsive seizures become so intense that they not only interfere with the taking of food but prevent sleep; and, if unchecked, psychic disturbances follow with elevations of temperature and

diffuse eruptions. Notwithstanding the differences of opinion in regard to the relation between chorea and the toxemias of pregnancy, the analogy in the symptoms and the pathologic findings in some of the cases should lead one to bear this relationship in mind and to keep these patients under close observation.

In a personal case, a para-ii, who gave a history of mild chorea during her first pregnancy, showed an entire absence of the characteristic movements during her nonpregnant condition. After the second pregnancy began, the choreic movements returned and continued throughout; being limited, however, to one side of the face, neck, and the arm. Labor was induced at term because the symptoms seemed to become a little worse. This was done successfully, although terminated by forceps. Within twenty-four hours a severe chill with considerable jaundice, increase in the convulsive movements and general restlessness was noted with elevations of temperature to 103° F. The incidence of the symptoms within a few hours after delivery and the absence of definite evidence of infection seemed to point to another cause for the same. Examination of the urine showed a moderate albumin reaction, although this could not be accepted as confirmative. The moderate jaundice lasted about twenty-four hours and then subsided. In contrast to this case another may be cited, which was seen a few weeks previously at the New York Lying-in Hospital. The patient, a para-iii, presented rather extreme choreic movements of the entire right side, for which labor was induced. There was no other disturbance present, and within a few hours after the delivery of a small, poorly-nourished child, the patient's symptoms rapidly disappeared. The child was successfully nursed. Chorea gravidarum is therefore a complication that must be carefully watched and its association with a possible toxemia kept in mind.

Differentiation of Eclampsia from Hysterical and Cerebral Convulsions.—Hysterical convulsions may occur during pregnancy as well as at any other time, but usually they may be differentiated from the convulsions of a toxic character by the absence of urinary signs, no loss of consciousness, and the absence of cyanosis and no tendency to lacerate the tongue. During labor, moreover, the attention of the patient is concentrated on her pains to such an extent that the hysterical seizures often disappear. True toxemia may also be present, and it is always well to exer-

cise care and judgment in making the diagnosis, as the more serious condition is otherwise overlooked. Convulsions due to a variety of cerebral lesions must also be taken into account. Tumors of various kinds involving the motor areas may produce symptoms that are difficult to distinguish from eclampsia.

The various convulsive manifestations, other than true eclampsia, that may occur during pregnancy are infrequent, however, when compared with the large number of cases of eclampsia ordinarily observed. Yet the points we have enumerated in the differential diagnosis should always be borne in mind in order that radical and perhaps unnecessary measures of treatment may not be instituted.

Increased Salivation.—The secretion of excessive quantities of saliva during pregnancy has been ascribed to a toxemia, although a neurosis, for want of a better term, is often assumed as the cause. Cases of increased salivation are apparently less frequent than formerly and I have personally seen very few that did not depend on some local irritating process in the mouth, such as jagged teeth or inflammation of the gums. The annoyance promptly ceased with the removal of this factor. In those severe cases reported in the literature as much as one or two pints of saliva have been noted. Little response to treatment occurred unless a definite toxemia could be established, when improvement followed eliminatory and dietetic procedures. Exhaustion of the patient will probably take place in the severer grades of the disturbance unless the pregnancy is terminated.

In cases associated with vomiting, improvement in salivation may be looked for with the subsidence of the symptoms of the former, which points to a toxic basis for these particular cases.

PRESUMABLE TOXEMIAS

Skin Eruptions.—Before concluding this chapter, attention must be directed to a group of symptoms not infrequently met with during pregnancy that are undoubtedly of a toxic origin in which skin eruptions are a characteristic feature. These are mainly of the dermatitis type, including various forms—impetigo, herpes, urticaria, erythema, and pruritus. These eruptions usually come on without warning and may be unaccompanied by other

symptoms, although questioning will usually elicit the reply that constipation or digestive disturbances have been present. As a rule the eruptions are transitory, although in cases of impetigo they may be very persistent, as in a case of Dr. A. B. Davis in the Lying-in Hospital, which presented on admission at the seventh month of pregnancy, an extensive impetigo involving the lower abdomen, legs, arms, and part of the face, including the lips. The woman's discomfort was extreme because the blebs had become infected. Fortunately labor could be induced by the administration of castor oil, and within a week after the delivery the symptoms had subsided almost completely. The administration of serum from pregnant or nonpregnant women, as well as that of animals, has been recommended for this purpose. Urticaria very frequently occurs in pregnancy and varies from the occasional appearance of small wheals to extensive eruptions covering the entire body. The eruption is usually found in individuals who develop it during the nonpregnant periods, and in such cases it is rather difficult to manage. As foreign protein is supposed to be the cause of the disturbance, if the specific protein can be determined, proper measures may be taken to relieve the patient.

Purpura.—Purpuric eruptions are sometimes noted in pregnancy, occurring either as occasional, isolated hemorrhagic spots in different parts of the body, or as a more severe manifestation associated with the advanced stages of pernicious vomiting or eclampsia. The former type is transitory, but in the other instance, the appearance of this symptom offers a grave prognosis. In such eruptions a differential diagnosis must be made between hemophilia and scurvy. Congenital hemophilia is rarely transmitted to females, but if there is a familial tendency, the vessel walls are undoubtedly more susceptible to the destructive action of pregnancy toxins. Scurvy is, of course, rarely met with among adults in this country.

Herpes.—Localized eruptions of herpes are not unusual, and ordinarily are of the vesicular or small bullous type. The lips and the extremities are usually affected, but occasionally the intercostal areas become involved and pain is annoying. Intestinal derangements ordinarily may be accepted as the cause, and when they are relieved the eruption generally subsides.

Pruritus.—Pruritus affecting particularly the genital regions, is a frequent manifestation in pregnancy which, if not due to an

evident local cause, may be accepted as an evidence of toxemia which subsides when the cause has been eliminated.

URTICARIA.—Urticaria constitutes a very annoying and not unusual complication of pregnancy, and may be ascribed to the increased vasomotor irritability during this period.

Angioneurotic Edema.—This is a condition that may be difficult to recognize, as it resembles, if occurring in the extremities, the ordinary subcutaneous edema so frequently found. The transitory character of the former is a conclusive feature, however, as is the fact that ordinary edematous areas are not limited to the extremities but may occur in any part of the body.

Prognosis in Toxemias of Pregnancy.—As regards prognosis in the various toxemias of pregnancy, a final summary may be introduced here. Taking up the different types and beginning with hyperemesis, we may safely say that even in moderately severe vomiting, the outlook is good so long as what may be called the nutritional balance is maintained. That is to say, if no great loss of body weight results, if the patient is able to be up a good part of the day, and the urine does not show any marked evidences of acidosis, the final outcome will usually be favorable. As a rule if the ordinary termination of the vomiting period is safely reached without abortion, the pregnancy proceeds without any after effects of the disturbance in the succeeding months. But if incessant nausea and vomiting is accompanied by rapid loss of weight and strength; if the vomitus contains coffee-ground material which denotes hemorrhages from mucous membranes; if jaundice, dry and coated tongue, and prostration are present; if bile pigments, albumin, casts, leucin or tyrosin, diacetic and oxybutyric acid and acetone appear in a urine of high specific gravity, then the outlook is serious, even if abortion is finally accomplished. The possibility of the recurrence of hyperemesis in subsequent pregnancies need not be considered in deciding on radical treatment. I have had several cases in which pregnancy was interrupted, which were entirely free from this complication in succeeding gestations.

In the presence of acute yellow atrophy of the liver the prognosis is invariably bad, and in nephritic toxemia only a prompt response to treatment should give other than a guarded prognosis. In nephritic as well as in pre-eclamptic toxemia, temporary alleviation of symptoms often lead to false hopes. The prognosis in eclampsia has already been referred to, but each individual case must be carefully studied and

the outcome based on the subsidence of symptoms or the appearance of the numerous complicating lesions already described.

Recurrence.—After the occurrence of severe toxemia in case of recovery, the question is often asked whether this complication will recur in the event of another pregnancy. Slemons reports a series of 18 personal cases in which more than one subsequent pregnancy occurred. In those patients who had suffered from toxemia in the latter months of the first pregnancy, fifteen had albuminuria only in the first pregnancy and in subsequent gestations they were free from the slightest symptom of toxemia and were delivered of healthy children. On the other hand, three suffered from this complication in each pregnancy. Two were twice pregnant and recovered, and the third died of nephritis several months after her fourth pregnancy had been terminated on account of pronounced albuminuria. It would seem, therefore, that out of six women who have suffered from albuminuria in the first pregnancy, only one may expect the complication to reappear.

Hospital Statistics as to.—Slemons' cases were all private patients, but hospital statistics show a large number of recurrences. Thus, Le Page found that 21 per cent suffered from similar symptoms in early pregnancies. From the records of the Johns Hopkins Hospital, Williams reports about the same proportion of recurrences, so that the same prognosis may be assumed. Slemons attempted to devise some means by which a possible prognosis could be formulated in such cases. Examination of the urine subsequent to delivery should be continued for some time and the estimation of the quantity of albumin is very helpful. Thus, if the albumin is reduced to a faint trace in the course of a week, permanent damage to the kidney is unlikely and the outlook for future pregnancies good. On the other hand, a measurable amount of albumin persisting over six or eight weeks offers a very gloomy prognosis, even though ultimately it disappears entirely. In such cases the kidneys are defective and, although they may be adequate for the requirements of health in the intervals between pregnancies, they begin to show signs of strain after the sixth month of gestation. Occasionally, rigid restrictions regarding diet and exercise serve to carry the patient to a point in the pregnancy where the fetus is viable; but as a rule the mother suffers from grave albuminuria and gives birth to a macerated or immature fetus.

When the disappearance of the albumin is less marked but persists for three or four weeks, the opinion as to the ultimate prognosis must be more doubtful. Some patients may pass through a pregnancy free from complications, but in others the toxemia will reappear. In the latter group the liver involvement must also be taken into account. The blood-pressure observations in such cases are of greater value than the albumin estimation, as a prompt drop will occur where the kidneys are not defective. Holste refers to an unusual case in which the patient was subject to eclamptic seizures during four successive years, the last one ending fatally. Although the patient had been under constant supervision and prophylactic treatment, nevertheless she developed convulsions. Operative delivery was necessary in every case. Autopsy showed extensive broncho-pneumonia with parenchymatous degeneration of the heart muscle and the liver. The kidneys seemed relatively slightly involved. In view of the predisposition to recurrent eclampsia in this patient, the writer believes that she should have been sterilized. Slemons also states in his article that he does not consider that the chemical methods for estimating the efficiency of the kidney have proved of any help in prognosis; in fact, it has been found that patients with a grave toxemia often eliminate the phenolsulphonephthalein given in the functional test more rapidly than healthy persons.

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CHAPTER III

PATHOLOGY

Hyperemesis—Hepatic lesions—Evidences of fetal origin—Renal lesions—Hemorrhages—Acute yellow atrophy—Differentiation from jaundice associated with severe hyperemesis and eclampsia—Nephritic and pre-eclamptic toxemias—Functional renal tests—Eclampsia—Renal and hepatic lesions—Hemorrhages—Cerebral edema—Ocular lesions—Placental infarcts—Other findings—Conclusions—Literature.

The preceding section, dealing with the etiology of pregnancy toxemias, presents, it must be admitted with regret, a picture dominated largely by uncertainty and speculation. This uncertainty has been correspondingly reflected in most efforts to place the pathology of these disorders on a satisfactory basis of established relations between cause and effect. After the idea that hyperemesis was a reflex or neurotic disturbance was dispelled by autopsy findings apparently closely resembling the lesions associated with eclampsia, a considerable period of time elapsed before the fact became established that well-marked differences exist between the pathological pictures underlying the toxemias of the earlier and the later months of pregnancy. The belief that the same or similar metabolic or other disturbances occurring at no matter what period of pregnancy, caused identical lesions in the liver and kidneys was not borne out by closer histological study. J. W. Williams, among others, has pointed out differences in the liver and kidney lesions at different periods and I believe it will be less confusing to base our consideration of the pathology of pregnancy toxemias on the clinical classification followed in the previous section.

The development of blood chemistry studies in toxemias has opened up an entirely new field of research within recent years which is of sufficient importance to warrant its consideration in a separate chapter. The urinary changes in pregnancies thus complicated have always occupied a great deal of attention, and while their study has been somewhat relegated to the background

by the advent of blood chemistry investigations, the subject will be given full consideration in a separate chapter.

HYPEREMESIS

Hepatic Lesions. — The pathologic lesions in the milder types of hyperemesis are quite unknown except as they may be

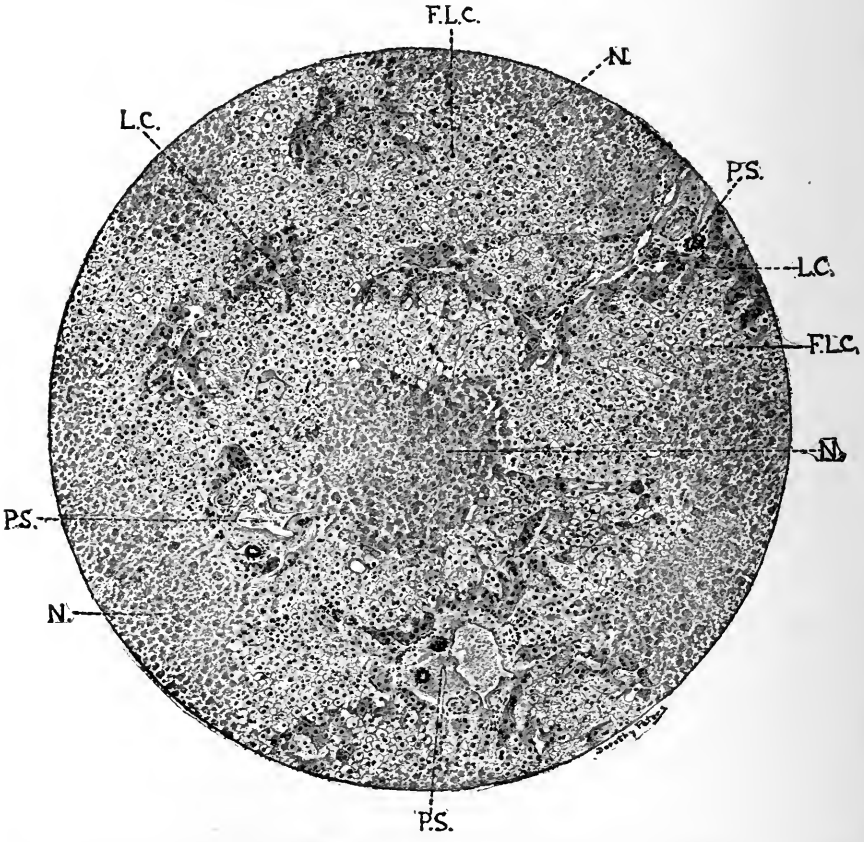

FIG. 10.—SECTION OF LIVER FROM A FATAL CASE OF VOMITING OF PREGNANCY SHOWING CENTRAL NECROSIS. *F*, *L*, *C*, liver cells showing fatty degeneration; *L*, *C*, unchanged liver cells; *N*, areas of necrosis; *P*, *S*, portal space (Williams).

interpreted from studies of the blood or urine. In the cases with fatal termination, the most characteristic organic change is to be found in the liver, which, first pointed out by Duncan in 1879, was later confirmed by Ewing, Stone and Williams in this country, and by Winter and Hofbauer in Germany. The hepatic lesion

resembles that found in acute yellow atrophy, and the most noteworthy and constant finding is a necrosis of the central lobules, the periphery remaining intact (Fig. 10). In this respect there is an essential difference, as Williams and others have pointed out, from the hepatic lesions associated with eclampsia where the process begins in the periportal spaces. The reduction in the size of the liver and the fatty degeneration of the cells often found make it doubtful whether such cases should not be regarded as true acute yellow atrophy. There is nothing specific about these findings for hyperemesis, although they are usually associated with the fatal cases, for similar lesions are found in fatal cases of phosphorus, arsenic, chloroform, and other poisonings by chemical substances. But these findings do point to the toxic character of the disease, and in severe cases where recovery has ensued, such lesions may at one time have been present, although recovery has obliterated all traces of their existence. We may assume their existence, however, from the urinary findings and it is possible that more precise functional tests directed to the blood as well as to the urine may reveal their presence.

Evidence of Fetal Origin.—That the circulating poison in hyperemesis, if such it is, is of fetal origin or stimulus, is evidenced by the fact that unless the organic changes have advanced beyond the reparative point, almost immediate recovery results from abortion or the death of the fetus. The fact that cases have been reported by Pick in which vomiting did not cease until all traces of secundines had been removed, would seem to point to the syncytial layer as the source of the poison and thus confirm Veit's theory of the migration of the placental villi. This theory is also apparently substantiated by the frequent association between hydatid mole and pernicious vomiting. Pinard reports a true hyperemesis in 19 instances out of 27 cases of hydatid mole, and Behm declared that in any case, chorionic villi might find their way into the maternal circulation and result in anaphylactic symptoms. No satisfactory histologic proof, however, has been brought forward to substantiate this theory.

Renal Lesions.—In addition to the lesions in the liver of fatal hyperemesis cases, more or less extensive changes in the kidneys, ranging from a simple exudate to a severe parenchymatous nephritis have been found. In fact, cases have been reported by Erisman in which renal lesions alone were found.

Hemorrhages.—Hemorrhages into the serous cavities and membranes have been observed in isolated cases by Schickele and bleeding from the gastric mucosa is quite common. Petechiæ in the serious cases are frequently seen and bleeding between the uterine wall and the fetal membranes is also found.

Interpretation of Findings.—An anatomical basis for hyperemesis might pardonably be assumed to be established from the extensive autopsy studies made by Williams, Stone, Ewing, Hirschberg, Marchand, Beatty and others, but Heinrichsdorf insists that these findings are not due to pregnancy toxemia, because of the prolonged course of the hyperemesis and the acute character of the organic lesions. He also claims that a similar pathologic picture is found in cases without any previous hyperemesis. In other words, an acute yellow atrophy of the liver is merely a complication of the toxemia and not a primary lesion preceding the latter. It seems reasonable to believe, however, that a common toxin underlies the hyperemesis and the later degenerative processes in the liver.

ACUTE YELLOW ATROPHY OF THE LIVER

Hepatic and Renal Lesions.—The pathologic picture to which this appellation has been given is confusing, but it undoubtedly is the terminal lesion in many fatal cases of toxemia which are ordinarily designated as hyperemesis or eclampsia. Preceded by jaundice, with or without other symptoms, the liver becomes tender and diminishes daily in size. This is accompanied by ecchymoses and the appearance of leucin and tyrosin crystals in the urine. The autopsy shows intense yellow staining of the body tissues and the liver may be only half its usual size. Marked fatty degeneration and necrosis of the hepatic cells is found in microscopic sections, especially of the central portions of the acini; in other words, an acute parenchymatous hepatitis. Degenerative processes are also present in the kidneys, involving the epithelial cells of the convoluted tubules, while the glomerular structures are but slightly changed.

Differentiation.—The pathological diagnosis in well-developed, typical cases of acute yellow atrophy is sharply marked, but in both hyperemesis and eclampsia, when jaundice appears and is

associated with the presence of leucin or tyrosin in the urine, the differentiation may be difficult and can only be determined by the autopsy. In eclampsia the liver changes, according to Heinrichsdorf and others, are focal, because they are believed to be due to thrombosis of the minute interlobular vessels and the peripheral capillaries, while in acute yellow atrophy the fatty degeneration

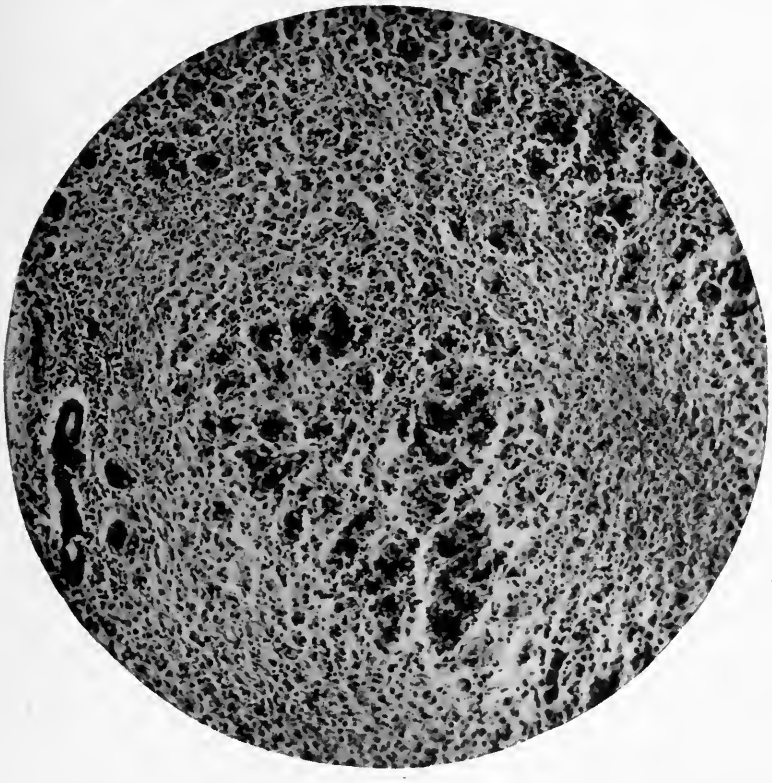

FIG. 11.—SECTION OF LIVER FROM A CASE OF ACUTE YELLOW ATROPHY, SHOWING DESTRUCTION OF ALL BUT A FEW GROUPS OF LIVER CELLS. (This and Figs. 12, 13, 19 and 20 were specially prepared by Prof. J. E. Ewing of Cornell University Medical College.)

and necrosis are diffuse. Moreover, a diminution in the size of the liver is not associated with either pernicious vomiting or eclampsia, although Heinrichsdorf asserts that the former is merely a rudimentary kind of acute yellow atrophy.

The clinical picture of hepatic degeneration is so constant in toxemias of pregnancy that we may refer at this point to a classification proposed by Seitz in which the gross pathological changes in the liver are differentiated as follows:

1. Toxic degeneration, characterized by diffuse fatty infiltration of the liver cells, without marked generalized necrosis and without contraction in the size of the organ, with a clinical picture of hyperemesis or general intoxication.

2. Acute yellow atrophy, marked by diffuse fatty degeneration with extensive necrosis and reduction in the size of the liver,

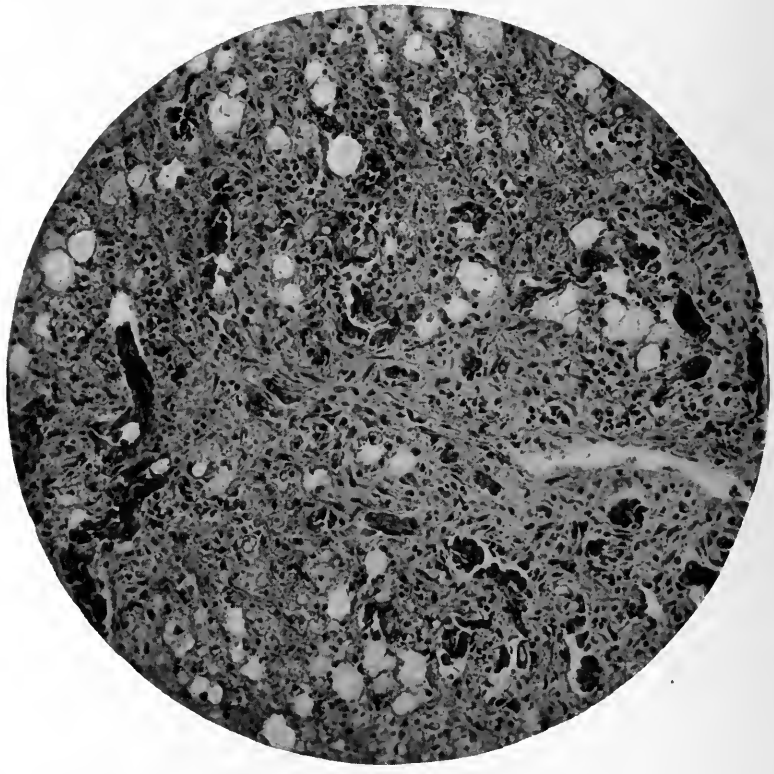

FIG. 12.—SECTION OF LIVER UNDER HIGH POWER OF A CASE OF ACUTE YELLOW ATROPHY, SHOWING FATTY DEGENERATION OF NECROSIS OF LIVER CELLS. Evidences of reparative process are seen in the replacement fibrosis. A few islands of darkly staining intact cells remain (Ewing).

characterized clinically by the well-known picture of acute yellow atrophy and frequently complicating a hyperemesis.

3. Eclampsia, characterized by focal cell degeneration and necrosis, as the result of thrombosis of the smallest vessels, is represented clinically by eclampsia with or without convulsions. Here we may add, there is no change in the size of the liver and subcapsular hemorrhages are common.

Schwangerschaftsleber.—The renal changes noted are not the only ones associated with pregnancy. As in the kidney, so we find minor alterations in the liver resulting from gestation, consisting of a mild degree of fatty infiltration and an alteration of function, a condition the Germans have called *Schwangerschaftsleber*, or pregnancy liver, which may by gradual transition lead to acute

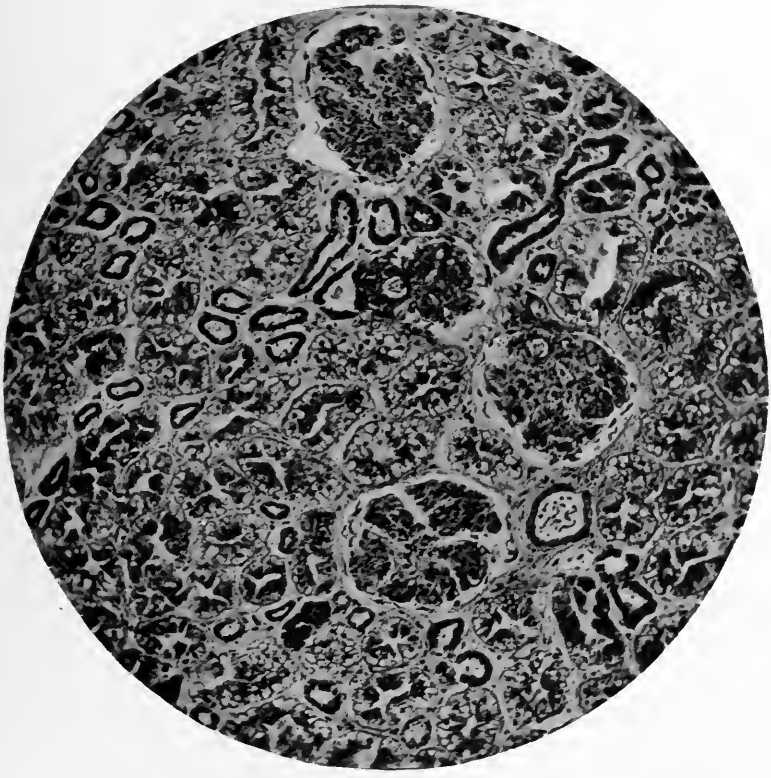

FIG. 13.—SECTION OF A KIDNEY FROM A CASE OF ACUTE YELLOW ATROPHY OF THE LIVER, SHOWING EXTENSIVE FATTY DEGENERATION OF THE LINING CELLS OF THE TUBULES (Ewing).

yellow atrophy or to eclampsia. The milder degrees of jaundice, "toxic icterus," often met with, are probably due to this pathologic condition. The resistance of the individual organs in any given case probably determines the effect of the toxin.

NEPHRITIC AND PRE-ECLAMPTIC TOXEMIAS

Pathology.—The pathology of these two toxemias may be considered with the pathology of eclampsia. The presence of an

albuminuria is so frequent in pregnancy that alterations in the kidney structure and its function, as well as that of the liver may be assumed to exist. When, however, mere traces of albumin become increased to 1 per cent, or more, and are associated with casts, particularly of the granular variety, a true kidney involvement may be suspected. In many of these cases exacerbations of an earlier nephritis may be at fault, and the differentiation may be difficult between an old and a new process. In the pregnancy kidney, however, the degenerative processes probably predominate, whereas in nephritis the inflammatory lesions are more prominent. In the former, the lesion involves the tubules and epithelium, leaving the glomeruli more or less free, and consequently a return to normal function occurs soon after labor.

Functional Renal Tests.—The histologic study of the kidneys in these types of pregnancy kidneys is scarcely satisfactory, because of the transitions found between various forms and the numerous gradations from one type to another. Functional kidney tests have been introduced to clear up the pathological physiology and it has been found that normal kidneys in pregnant women excrete water, sodium chlorid and nitrogen equally as well as in the nonpregnant. In the presence of renal disturbances associated with pregnancy, the excretion of water and chlorids is diminished, although the nitrogen is unchanged. This insufficiency often goes hand in hand with the percentage of albumin, although not invariably. Care must be taken in interpreting the pathology of the kidneys by these tests, but in many instances the results are of value in determining a pre-eclamptic toxemia before edema or other signs appear.

ECLAMPSIA

Renal Lesions.—The pathologic studies of this most serious complication of pregnancy have not been productive of any final opinion which might definitely establish the etiology of the condition.

Since the constant association between albuminuria and eclampsia was first brought to the attention of the profession by Lever in 1843 the importance of kidney lesions has always been dwelt upon. In fact, the convulsions and the coma associated with eclampsia correspond so closely to the convulsions of

nephritis that for a long time they were supposed to be one and the same thing. More thorough histological studies have shown, however, that the kidneys of eclampsia present an entirely different anatomical picture. A chronic interstitial inflammation with constriction, obliteration of the cortex and the vessels, diminution in size and sclerosis are the predominant characters of the kidney

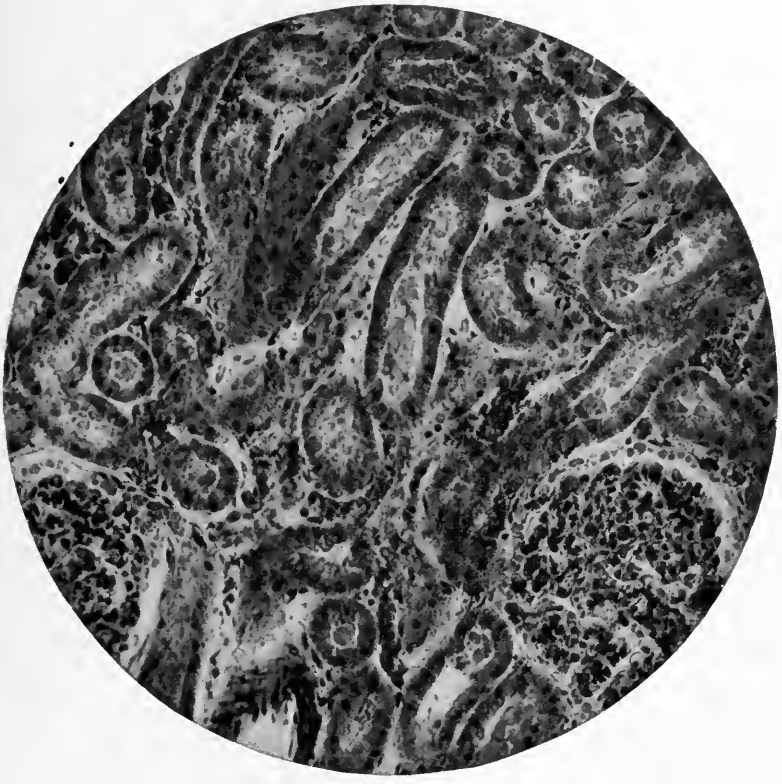

FIG. 14.—SECTION OF KIDNEY FROM A CASE OF ECLAMPSIA SHOWING ACUTE PARENCHYMATOUS LESIONS—High Power (Hull).

of nephritis. In eclampsia, on the other hand, the kidney is not diminished in size, the appearance is anemic, the cortex cloudy and in many instances presents small punctate ecchymoses. The capsule, as a rule, is not adherent. A microscopic examination shows degenerative changes in the epithelium and vessels. The epithelium of the damaged urinary tubules is apt to be disintegrated, swollen and deprived of nuclei. The capillary vessels are filled with red cells showing a marked vascular stasis and may also contain actual thrombi. The interstitial tissues of the kidney

seem to be little changed and the process involves almost entirely the parenchyma of the organs. Infarcts may be present and are due to the migration of emboli from other organs.

In a collection of 368 autopsies after eclampsia made by Prutz, involvement of the kidneys was stated to be present in all but seven, and these findings were confirmed by Pollak of Vienna,

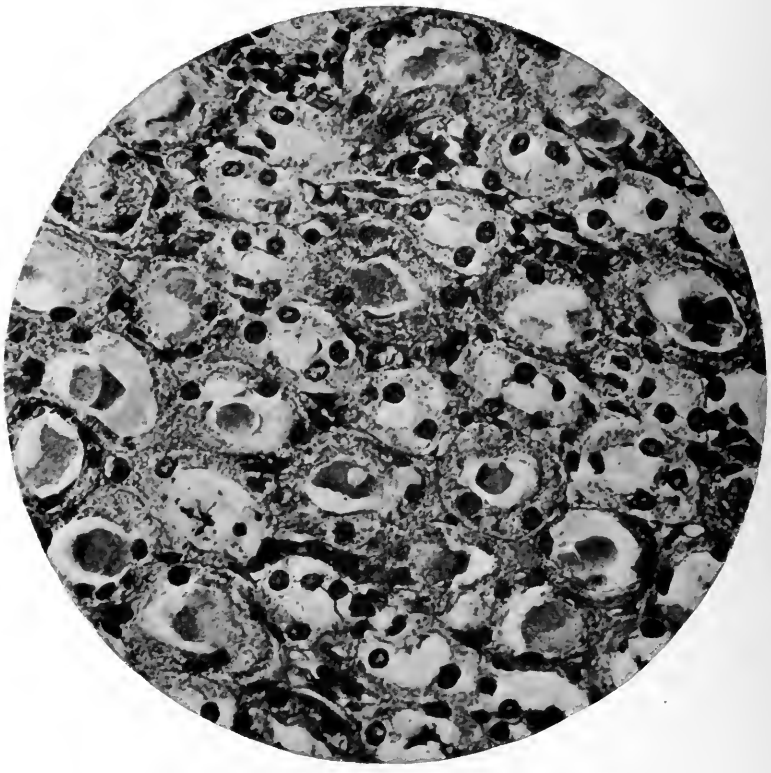

Fig. 15.—Section of Kidney from a Case of Eclampsia Showing Tubules Filled with Hyaline and Granular Detritus. The lining cells in places have almost entirely disappeared (Hull).

who noted renal changes in 98 per cent of 139 autopsies of eclampsia cases.

Hepatic Lesions.—So much attention was given to the study of renal pathology in eclampsia that lesions in other organs were strangely overlooked. Although Virchow and Scanzoni both referred to the frequency of liver involvement, the characteristic pathological changes in the liver of eclampsia cases were first definitely made known by the observations of Pilliet and Letienne

and by Schmorl. The liver in gross appearance presents irregular hemorrhagic areas sometimes of large extent. On section there are patches of alternating light and dark areas which give a mottled appearance to the organ. Section shows a necrosis in the lobules and portal spaces, which has been attributed to thrombosis in the small portal vessels with consequent degeneration (Fig. 18).

In Schmorl's series of cases this condition was invariably

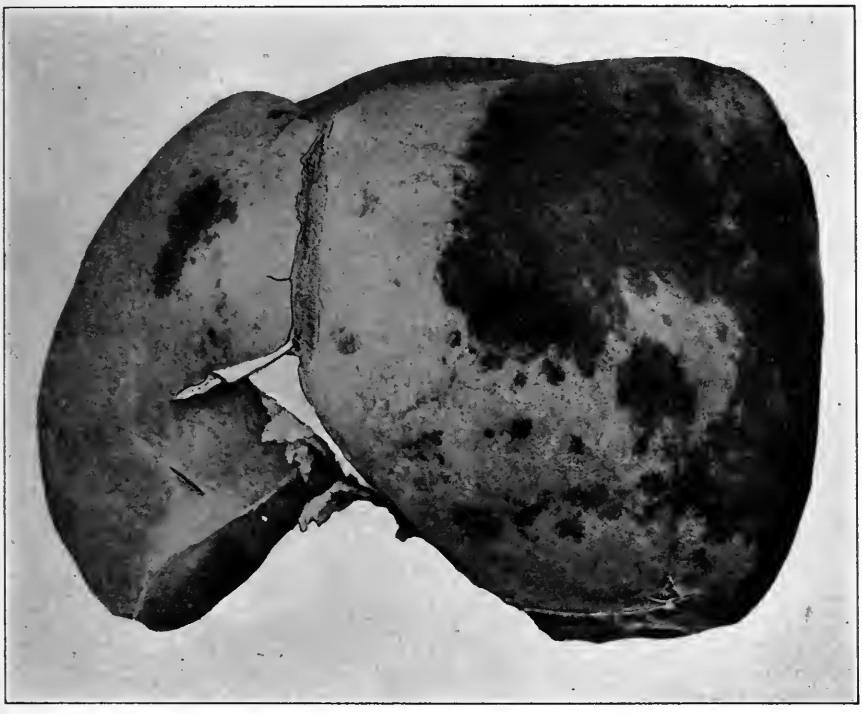

Fig. 16.—Liver from an Eclamptic (Same Case as Fig. 20), Showing Extensive Diffuse Subcapsular Hemorrhage. Also numerous scattered hemorrhages in the substance with cloudy swelling of the parenchyma. There was no cirrhosis or arteriosclerosis present.

present; and according to this author, the change is neither inflammatory nor a fatty degeneration, but, as he says, an anemia or hemorrhagic necrosis which is especially well marked in the region of the suspensory ligament. Closer microscopic study seems to demonstrate the origin of the process in the periportal connective tissue, so that the periphery rather than the center of the acini is involved.

Histology.—Konstantinowitsch, in describing the histology of the process, states that the earliest change in the liver of eclampsia is an alteration in the liver cells and the endothelium of the capillaries in the peripheral portion of the lobules. This alteration increases with the progress of the disease, until the liver cells present a reticulated, vacuolar appearance. At the same time dilatation and congestion of the capillaries on the peripheral portion of the lobules appears, which are due to an impeded circulation from primary thrombosis of the vessels in this part. A necrosis of the hepatic cells results.

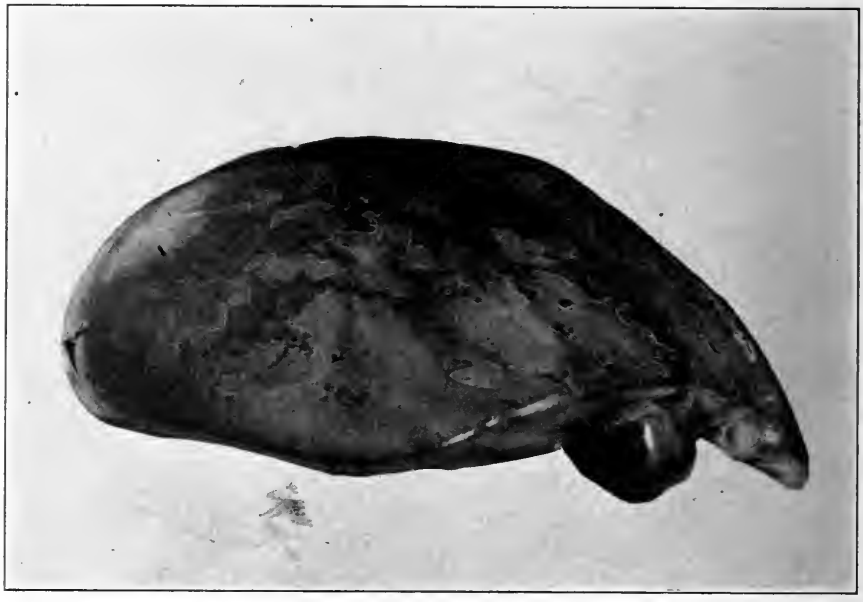

Fig. 17.—Liver from a Case of Eclampsia Showing Extended Distribution of Subcapsular Hemorrhages (case from the N. Y. Lying-in Hospital).

There is apparently no relation between the extent of the necrotic process and the severity of the convulsive seizures, for Schmorl reports one case with twenty-six convulsions in twenty-four hours, in which the necrotic areas were few and widely scattered, while in another case where death took place forty minutes after the only convulsion, about one half of the liver parenchyma was necrotic. Three other cases are reported in which similar changes were present without any convulsions, and such findings may account for fatalities where no evidence of disease was previously noted.

Another important contribution to the subject is a report by Welch of the autopsy findings in 12 cases. Welch divides the liver lesions found into four classes. The first includes hemorrhagic changes in and about the portal spaces. This condition was found in 6 cases, 2 of which had no convulsions. The second class

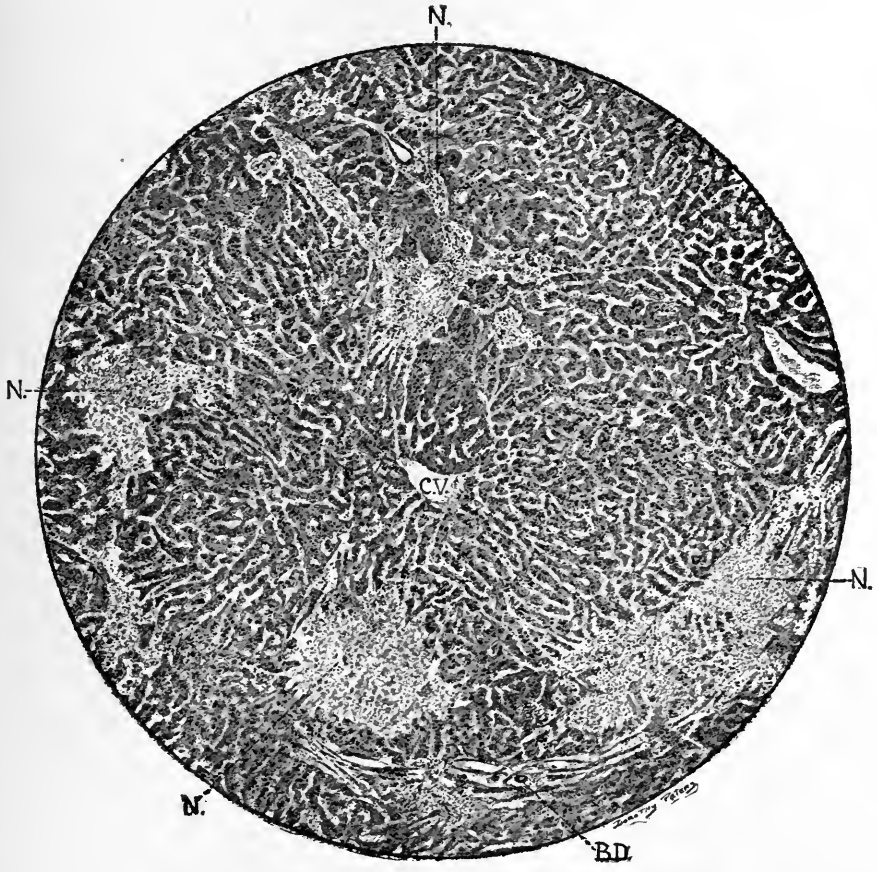

Fig. 18.—Cross-section of Liver from a Case of Eclampsia Showing Periportal Necrosis at N (Williams).

includes 3 cases which showed necrosis in the center of the liver lobule. These cases were diagnosed clinically as eclampsia. The third class includes only 1 case, in which there was no hemorrhage but a general swelling of the cells, with autolysis. The fourth class includes 2 cases in which the liver alteration was a very slight, cloudy swelling of the parenchyma with no hemorrhage or necrosis. The kidneys in the last class show extensive disintegra-

tion of the epithelium to about the same degree as was found in the kidneys of the other three classes.

The kidney lesions were similar in all the cases. In none was the lesion a uniform one. The parenchyma was affected throughout, but in some parts of a given kidney more destruction was present than in other parts of the same organ. Welch

FIG. 19.—SECTION OF LIVER FROM A CASE OF ECLAMPSIA UNDER HIGH POWER. Shows thrombosis and necrosis of the hepatic arterioles, with infarcts of the surrounding liver cells (Ewing).

believes that the hemorrhages and necroses are not due to thrombi resulting from hyaline blood plates or from giant cell emboli in the liver parenchyma, as explained by the earlier investigators. Although all of these have been found in certain instances, it would be difficult to imagine that the extensive hemorrhages so commonly found throughout the body in eclampsia are due to multiple emboli.

Welch found that most of his cases showed considerable

hemolysis. The masses described as fibrin in the hemorrhages of the liver do not appear as clear-cut fibrin fibrils, but have a hyaline appearance which in places appeared like fused red blood-

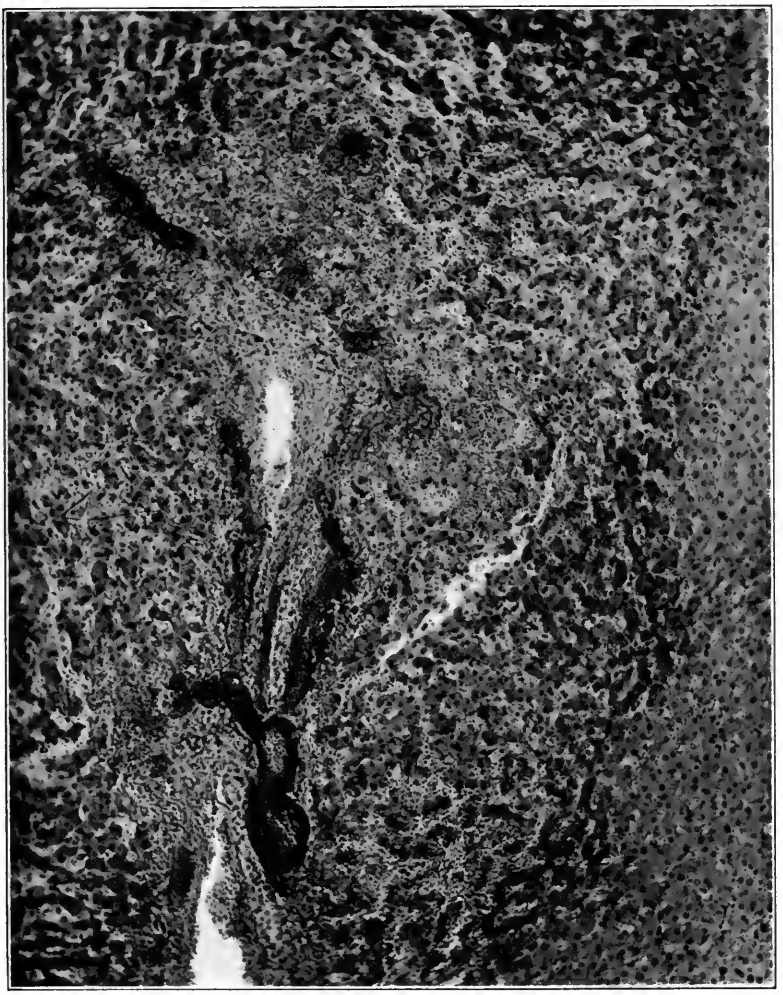

FIG. 20.—SECTION OF A LIVER FROM A CASE OF ECLAMPSIA. Shows the process of thrombosis of the periportal vessels and necrosis of the liver cells at the periphery of the lobule (Ewing).

cell stroma. There were also found within the vessels agglutinated red cells fused into hyaline appearing masses. As it has been shown by experiment that hemolysis from the action of poisons is first preceded by agglutination and fusion of the red cells before

they undergo solution and give up their hemoglobin, Welch believes it is possible that the condition found in the parenchyma cells indicates the action of some dissolving poison. He asserts that the latter can also attack the endothelium of the blood vessels and that the hemorrhages may be explained through these agencies. The reason that the hemorrhages are more numerous in the liver is because the toxin in the blood is reënforced by that of the liver. If to these causes we add the increased blood-pressure which is usually found, the large brain hemorrhages may be accounted for, for these occur in young subjects who are usually free from arteriosclerosis. Welch claims that the poison which causes such serious intoxication is probably an enzyme or a combination of enzymes. If these enzymes are distributed in some hitherto unknown manner they will attack the cells in which they reside and cause their destruction, or, in other words, the process known as autolysis will take place. As the liver cells are especially rich in these enzymes, the greatest destruction occurs at this point.

Hemorrhages.—Although kidneys and liver present the most frequent and most characteristic pathologic changes at autopsy, almost all the organs may be more or less involved. Hemorrhages may take place into the lungs and pleura, pericardium, cranial cavity and brain, gastric mucosa, peritoneum and skin. Welch in his series reports a cloudy swelling of all the involved organs, most easily seen in the heart muscle and other unstriped muscles throughout the body. Marked hemolysis is to be observed in these cases, and there is usually more or less effused blood in the body cavities, colored by the blood pigment liberated by the process.

Pulmonary thrombosis has frequently been observed, marked by the finding of "giant cells" in the capillaries, which are supposedly of placental origin. The fact that such emboli are found in pregnant women dying of other diseases contradicts the claim that they are the cause of the thrombotic processes. Fat emboli also occur in the lungs but are probably not of pathological origin, being derived from the normal fat deposits in the subcutaneous or connective tissues and the bone marrow. They probably result from the convulsions. Bronchopneumonia and an extensive pulmonary edema are often found in cases progressing to a fatal ending several days after convulsions have ceased. There is

nothing characteristic in such lesions, nor in the development of septicemic foci sometimes found.

Hemorrhagic lesions in the brain have been noted in most autopsies in eclamptic subjects, both substance and cortex being involved (Figs. 21, 22). In addition diffused areas of cortical softening are frequently observed as well as edema or hyperemia, al-

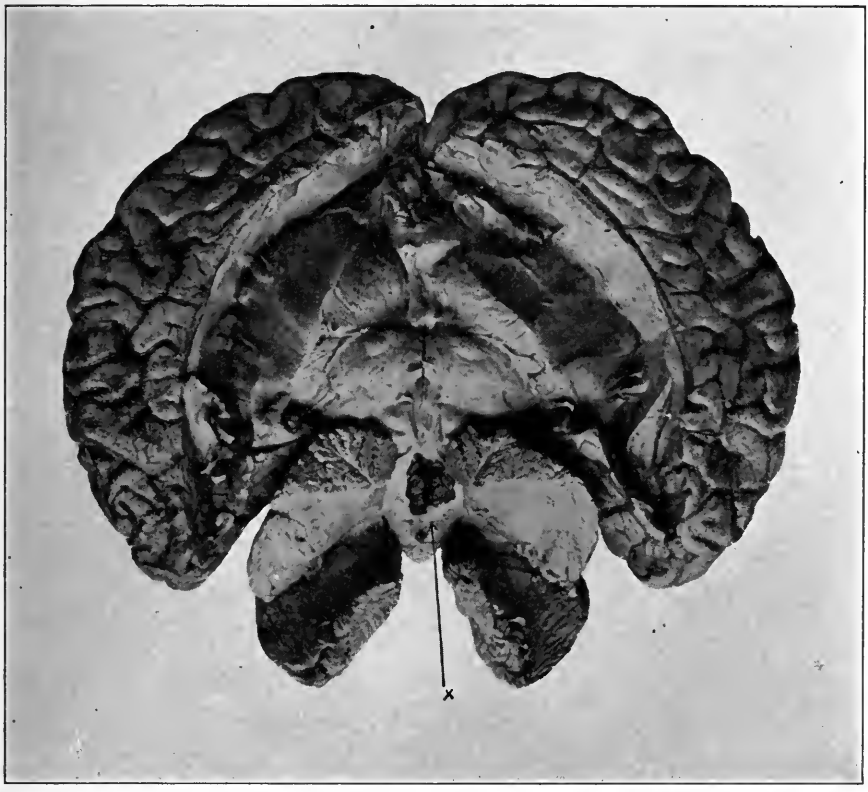

FIG. 21.—VIEW OF THE BRAIN LAID OPEN. FROM A CASE OF POST-PARTUM ECLAMPSIA IN A PRIMIPARA IN ECLAMPSIA WITH A SINGLE CONVULSION. The ventricles were distended with blood and many petechial hemorrhages were scattered over the surface. In the lower part of the pons a hemorrhage ruptured into the fourth ventricle. The vessel walls in this specimen all showed a cloudy swelling indicating the probable acute action of a circulating toxic substance. The liver from this case is shown in Fig. 16 (N. Y. Lying-in Hospital case).

though edema is probably not reported as often as it occurs, because of its rapid subsidence after death. The hemorrhages are probably thrombotic in most instances but, as Welch has pointed out, the vessels may rupture as the result of the solvent action on the

endothelial lining by a circulating toxic enzyme aided by the increased blood-pressure. The extent of the bleeding varies from that of small degree in the pons, as shown in Fig. 20, to an extensive effusion into the lateral ventricals (Fig. 21), which distends their cavities and lacerates the walls. True cerebral apoplexies are also found, usually in the distribution of the middle temporal artery; and in those cases of eclampsia where hemi-

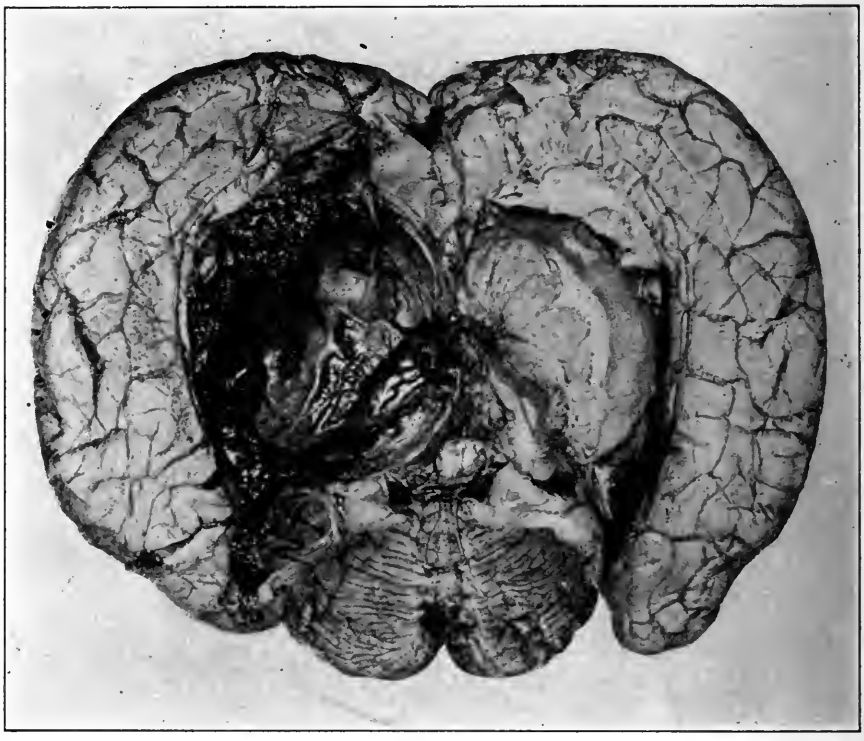

FIG. 22.—BRAIN LAID OPEN. FROM A CASE OF ECLAMPSIA WITH CONVULSIONS. Shows extensive traumatic hemorrhage into the fourth ventricle (case from the N. Y. Lying-in Hospital).

plegia or other paralytic lesions develop, cortical hemorrhages in the motor areas have probably occurred, with or without recovery. The high blood-pressure associated with the disease predisposes to the occurrence of these hemorrhages, but since venesection has been revived a reduction in the incidence of this lesion has been observed.

Cerebral Edema.—Edema of the brain, with its resultant intracranial pressure, is declared by Zangemeister to be the cause of

eclampsia. He diagnosed this edema as an actual "glaucoma of the brain," and, in three severe cases, attempted to relieve the tension by prompt osteoplastic resection of the skull. After turning back a bone flap on the right side above and behind the temple, the dura was found hard and tense, the pressure being so great that there was no pulsation. Large quantities of serous fluid escaped after incising the dura and the convulsions subsided. Two of the three patients recovered. One of the cases in which the dura was sutured died on the sixth day, and Zangemeister believed that the edema probably recurred.

Hemorrhage of Heart and Other Organs.—The heart in fatal eclampsias shows, on examination, hemorrhages into its substance, together with areas of necrosis and albuminoid degeneration of the muscle fibers. Hemorrhagic and necrotic areas are less frequent in the pancreas and suprarenal bodies.

Traumatic Lesions.—The serious character of traumata to internal organs that may take place in eclampsia is well shown in the report of a case by Lobenstine and Welch. The patient, a primipara, developed severe convulsions about eight hours after delivery which were succeeded by a condition of coma with a fatal issue twenty-four hours later. The autopsy showed in addition to the usual lesions in the internal organs, an extensive rupture of the diaphragm and several perforations of the posterior wall of the stomach. The mucous membrane of the latter was markedly congested and contained many small hemorrhages. These ruptures probably occurred during the period of convulsions, although the patient apparently survived them several hours. Traumatism from treatment could be excluded in this case.

That pregnancy toxemias predispose to uterine hemorrhages among other complications, has been shown in several investigations. Thus, Davis-Colby demonstrated in a series of cases that such bleeding often constitutes the chief symptom. He proposed the following classification for hemorrhages associated with toxemia: (1) Hemorrhage from the kidney. Of 36 cases with eclampsia, hematuria was present in 10, of which 6 died. (2) Hemorrhage from the uterus. In 13 cases of accidental hemorrhage there were 8 which showed unmistakable evidences of toxemia; whereas where external bleeding took place, as from placenta praevia, there was only one instance of toxemia in 30

cases. (3) Purpura and bleeding from the mucous membranes, in which the prognosis must be regarded as unfavorable.

Smyly also inclines to the opinion that most cases of severe, and especially of concealed, internal hemorrhage are due to toxemia and will usually be found associated with albuminuria and other symptoms of this condition. Smyly also calls attention to the fact that when cesarean section is performed in these cases, the blood will be found not only in the uterine cavity but also in its wall, separating and injuring the muscle cells. Hemorrhage into the pelvic cellular tissue between the folds of the broad ligament and in the peritoneal cavity itself has also been noted in such cases. When premature separation of the placenta occurs, edema of the uterine walls is frequently observed and in a series of 8 cases reported by the author at a meeting of the Royal Society of Medicine in 1916, albuminuria was present in every instance. In 5 of this series, moreover, a large hematoma in the broad ligament was found, and in 2 others, there was free blood in the peritoneal cavity. In these cases not only was the placenta more or less detached and the uterine cavity filled with blood, but blood was also extravasated into the uterine walls, especially under the peritoneal coat.

Ocular Lesions.—The frequency of visual disturbances should have inspired numerous studies in the pathology of the eye in eclampsia, but few references are available. In addition to more or less diffused retinal hemorrhages, actual rupture of the retina may occur, as shown in a report by Schiotz, who presents the records of three cases of retinal detachment during pregnancy with nephritis. The patients were primiparae, seventeen, twenty-nine, and thirty-five years of age respectively, with albuminuria and convulsions, but without pronounced edema. The detachment occurred after several convulsions. In the oldest case at the seventh month of pregnancy it was bilateral, and persisted for a month after labor, when a return to the normal resulted. In a subsequent pregnancy five years later, no visual disturbances were noted. In the twenty-nine-year-old patient there was also retinitis and detachment which persisted for two weeks until delivery at the seventh month, when the retina returned to place. The youngest patient developed convulsions after delivery at term and the detachment occurred without any retinitis and persisted.

Placental Infarcts.—The theory that eclampsia is caused by a placental poison has directed attention to the anatomical study of this organ, in which infarcts and hemorrhages have been so frequently observed. Placental infarcts are said to stand in a direct relation to albuminuria and toxemia by a number of investigators (Holland for one), although whether as a cause or a consequence does not appear to be definitely settled. The condition may undoubtedly exist without any evidences of toxemia and the contrary also holds good. Williams found in his series of cases that infarct formation is not particularly marked in acute cases of eclampsia, but is usually observed where marked albuminuric symptoms are present. Young, who has contributed a classical study on this subject, believes that in acute toxemia ending rapidly in labor, the placenta may present evidences of disease or look perfectly normal to the naked eye. If, on the other hand, the acute attack passes off and labor supervenes ten to fourteen days later, extensive recent necrosis will be found. Young regards this fact as sufficient evidence of the causative rôle of autolytic changes in the affected organ. He proceeds to demonstrate this by anatomical data and experimental results. I consider the matter of importance enough from the pathologic standpoint to warrant a somewhat detailed presentation of his view because of its bearing on the etiology of eclampsia.

Origin.—In attempting an explanation of the cause of placental infarction, Young directs attention to the very loose connection between the fully developed placenta and the uterine wall—a thin decidual film being all that binds the two together. This film bridges across the large venous channels, so that the placenta seems to rest on a greatly expanded blood lake. Where the vessels perforate the placenta the film is absent and there are other places where the villi dip deeply into the blood spaces. Veit believed that deportation of the villi occurred through these openings into the blood stream. Although this anatomical arrangement provides for ease of separation, it also affords an opportunity for vascular disturbance including the formation of placental infarcts. It may be remarked in passing that there are two theories regarding the origin of the latter:

1. Eden, Williams and others believe that placental infarct is due to a change commencing primarily in the villi themselves. The blood supply is interfered with as the result of an obliterating

change in the vessels, which leads to a degeneration of the epithelium and stroma of the villi, and, secondarily, to a coagulation of the maternal blood.

2. According to another theory the degeneration is due to an interference with the maternal blood supply. Let us quote Young directly in discussing these theories:

"The first, the most commonly accepted idea naturally assumed that the villi are dependent for their nourishment upon the fetal blood supply, and that once this is obstructed they must undergo progressive necrosis. If one could show definitely that the villous structures are independent of the fetal blood, and, moreover, can live and proliferate when this is removed, so long as the maternal supply remains intact, it would render this explanation of the infarction process untenable. This is not difficult to do. There are several considerations which show it:

"(1) The time when the chorionic elements are most active and proliferate most rapidly is during the early stages of the development of the ovum, where there are, as yet, no fetal vessels formed, and where the trophoblast and its villi obviously live directly upon the mother's blood.

"(2) In hydatid mole the chorionic villi live, and, as we know, actively proliferate, when there is not a trace of a fetal vessel, and when the entire nourishment is derived from the blood of the mother. The same is true of chorionepithelioma.

"(3) In tubal pregnancy one can sometimes recognize the independence of the villi of the fetal blood in a diagrammatic manner. Where there has been a considerable hemorrhage into the extrachorionic space great masses of villi become strangled in blood-clot. I have seen one such case where all the trunks in the neighborhood of the chorion had undergone fibrinous necrosis, but near the tube wall, where, in parts, the maternal circulation was unimpaired, the tips of the necrotic villi remained healthy.

"These facts demonstrate beyond doubt that the villi, even after the fetal blood supply is removed, can live, so long as the maternal supply remains uninvolved."

It is evident, if this reasoning is correct, that localized patches of dead placental tissue result from an interference with the

maternal blood supply; for, as Young pointed out elsewhere, in by far the largest number of cases, infarcted areas lie in close relation to the decidual surface, and in such cases degeneration, often necrosis, of the decidua may be detected. Furthermore, small nodules of healthy placenta may sometimes be seen on the decidual aspect of large infarcts, which means, according to Young, that whereas the remainder of the infarcted portion has lost its nourishment, the healthy nodule has retained its maternal supply. This, however, is admitted to be a rare occurrence.

Young believes that another convincing proof of the maternal origin of infarcts lies in the changes associated with placental hemorrhage, for where retroplacental hemorrhage has resulted, the adjoining placenta is diseased, provided a certain time has elapsed.

Young contends that the interference of the blood supply which is responsible for the infarction is not dependent upon a toxic state, and, in point of fact, may occur in the most extreme form where there is no evidence of a toxemia, as for example, in accidental hemorrhage. Furthermore, the placenta is so constructed that if a part of it dies, the products liberated from the dying patch can pass directly into the blood stream. It is apparently necessary, therefore, from the anatomic standpoint, that, for the occurrence of a toxemia, the blood must circulate around the poison-generating foci. Young believes that an understanding of this fact at once dispels many of the difficulties associated with the study of this condition. It explains, for example, the cessation of symptoms after the death of the child and the separation of the placenta and also explains the absence of a toxemia in cases of accidental hemorrhage in which the placenta is completely detached by the blood-clot. The cases of accidental hemorrhage associated with toxemia are those in which part of the placenta remains attached for some time after the separation of the adjacent portion by the retroplacental bleeding. It is the necrosis of this part which liberates the toxic materials. These facts, according to Young, suggest that the toxemias are due to the autolytic products liberated in the early stages of placental death (see Figs. 6, 7, 8, 9). He attempted to imitate this process, which occurs *in utero*, by isolating from the healthy placenta the soluble substances which reproduce the clinical features and morbid changes characteristic of eclampsia, including convulsions, peripheral focal

necrosis in the liver and degenerative lesions in the convoluted tubules of the kidney. The occurrence of post-partum eclampsia is in apparent opposition to this theory, but Young believes that even small pieces of retained placenta may act in the manner described above.

Experimental reproduction of eclampsia was carried out in guinea pigs. Carefully prepared dry, powdered placenta and glycerin extracts of placenta were administered subcutaneously in varying doses to 47 animals. Severe and prolonged muscular spasms developed within less than a minute, accurately reproducing an eclamptic seizure. The placental powder seemed to be the most effective in producing symptoms and death usually occurred in these cases. Autopsies showed typical degenerative lesions in the liver with similar but less marked examples in the kidneys. The glycerin extracts seemed to produce even more marked necrotic changes, although the convulsive symptoms were absent, or less marked. This condition seems to correspond with the clinical differences observed in eclampsia in the human subject where convulsions are the chief symptom in one group, whereas they may be absent in the other, although in each case the resulting pathological lesions seem to be the same. Further investigation in the directions referred to in Young's article may lead to a more satisfactory knowledge regarding certain fields of investigation in eclampsia which have hitherto been apparently neglected.

Differential Diagnosis.—The differential diagnosis between eclampsia and other conditions characterized by convulsive seizures is often only made at autopsy. Thus Croom reports 2 cases which closely simulated eclampsia but in both of which the urinary changes were entirely absent. In one instance there was a large tumor of the left anterior parietal region, fatty and catarrhal changes in the kidneys, and fatty degeneration of the liver and heart. The tumor consisted essentially of epithelium with a supporting stroma of connective tissue. There were no symptoms directly referable to the cerebral neoplasm and death was apparently due to eclampsia. In the second case a similar train of symptoms was found to be due to tubercular meningitis.

Conclusion.—Summing up the autopsy findings of eclampsia we note that the most constant lesions are hemorrhage, principally in the liver, and degenerative processes which involve any one or nearly all of the essential internal organs. Their distribution, extent and individual characteristics vary widely and the

paucity in certain fatal cases with few clinical symptoms and their frequency in others would make it appear that their presence is secondary to the presence in the circulation of some toxic substance. The nature of this toxic substance is still unknown, but it seems to predispose to hemorrhage through its possibly solvent action on the endothelial lining of the blood vessels, as pointed out by several observers. That this toxic material may possibly be transmitted to the fetus seems a reasonable supposition, as similar lesions are found after death in the babies of eclamptic mothers. These babies usually die in convulsions, within the first few days after birth.

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CHAPTER IV

TREATMENT

Treatment of hyperemesis—Physical examination—Correction of uterine displacements and stenoses—Cauterization of cervical erosions—Diet—Corpus lutein extract—Laxatives—Rest—Routine care—Rectal—Emptying the uterus—Supplementary measures—Acute yellow atrophy—Nephritis and eclampsia—Prophylactic measures—Constipation—Care of organs of elimination—Blood-pressure observations—Visual disturbances—Treatment of convulsions—Induction of labor—Rectal infusions—Post-partum care—Urine examinations—Summary of specific plan of treatment—Conservative and radical venesection—Skull trephining and lumbar puncture—Infusions of magnesium sulphate—Ductless gland therapy—Necessity for carbohydrates—Intravenous injections of glucose—Literature.

General.—In any endeavor to describe the treatment of the various toxemias of pregnancy, the cardinal fact to be borne in mind is, that no routine method applicable to any or all classes of cases can be recommended, but that in each instance, particularly in the severer types, consideration must be given to the individual patient. In this connection I am reminded of a comment made by the late Professor Delafield of the College of Physicians and Surgeons in New York when lecturing on the treatment of pneumonia: "Always," he cautioned his students, "treat the patient and not the disease." This warning can be applied equally well to the subject matter in hand and my personal experience prompts me to preface the description of the treatment of these disorders by the insistence that each case of toxemia be treated individually and that, while we can follow certain general and well-recognized routine procedures in certain groups of cases, they must be changed as circumstances may dictate. In order to apply such individual treatment the underlying etiological factors should be determined, if possible, so that an intelligent handling of the case can be undertaken. For example, in the vomiting of early pregnancy, the possible reflex or anatomical causes must be carefully sought out before instituting treatment, because if they are present the case cannot be regarded from the toxic standpoint alone,

but must be treated with the measures which have been recommended for this type of vomiting. Nor in the toxemias associated with the latter months of pregnancy, is every woman who presents a headache, or pain in the pit of the stomach, to be regarded as a possible eclamptic, nor should every case in which convulsive movements occur be subjected to the eliminatory treatment proper for true eclampsia. The differentiation of these conditions has already been considered in the section of Symptomatology.

The general subject of the treatment of toxemias of pregnancy will be considered under two main divisions: That relating to the disorders of the early months as manifested by excessive vomiting and that dealing with toxemias associated with the latter months and generally known as eclampsia.

TREAMENT OF HYPEREMESIS

Physical Examination.—A patient presenting herself with a history of vomiting associated with amenorrhea, should first of all be subjected to a careful general physical examination. After this has been done and the condition of the heart, lungs, kidneys, digestive system, etc., determined, a careful pelvic examination should make known the position of the uterus, the condition of the cervix and other deviations from the normal. The association of definite mechanical or pathological findings should prompt immediate attention to their correction. Malpositions of the uterus are frequently associated with the nausea and vomiting of pregnancy. If a retroverted uterus is found in a primipara we may accept this as the congenitally normal position of the organ and attempts at correction are often a failure and become very distressing and painful until the uterus is large enough to come out of the pelvis. It is unnecessary to attempt the correction of this deformity in a woman in whom such a position is the normal one, and we know that in a certain number of cases the uterus is in a retroverted or retroflexed position. In a woman who has borne children, however, retroflexion may be acquired, and if so, it is ordinarily a simple matter to replace the organ, if it is not adherent.

Retroflexion, Correction of.—I have not been impressed with the necessity for the correction of retroflexion unless the fundus of the

uterus gets caught under the promontory of the sacrum in about the fourth month when, in addition to the nausea and vomiting, there is usually present the associated symptom of pain. In order to relieve the uterus from its fixed position in such cases it is necessary to place the patient in the knee-chest posture and then, with a bivalve speculum exposing the cervix, the anterior lip is seized with a strong double tenaculum forceps and by traction efforts an attempt is made to release the fundus from its impacted position, aided by the fingers in the vagina. Before doing this, the patient should first be advised to assume the knee-chest position at daily intervals and not to lie upon her back while resting. I have seen several cases in which a retroposed or retroverted uterus was restored to an anterior position without further manipulation. A uterus of this size cannot be held in place by a pessary with any degree of comfort.

In the earlier months, however, if a retroversion is determined to be pathological and it is possible to replace the organ, the ordinary retroversion pessary may be worn by the patient until the fundus rises above the pelvic brim. One should exercise care, however, in its introduction, and remove it at intervals of two or three weeks for cleansing. If any pain or discomfort results the pessary must be removed at once and preferably no further attempts made to use it for this purpose. The patient should also be directed to douche at least twice a week, with warm water containing a teaspoonful of powdered borax to two quarts, employing for the purpose a glass douche nozzle which is thoroughly cleansed after use and kept in a folded fresh towel. It is advisable, especially where a vaginal discharge is present, to make a visual examination of the cervix through a bivalve speculum.

Hyperemesis has been attributed to any one of a number of cervical lesions, including stenosis, erosions, chronic inflammations of the canal, and lacerations.

Stenosis of Cervical Canal.—Dilatation of the canal with graduated sounds at daily intervals has been suggested, the dilatation being carried on until relief from symptoms results. It is asserted that this procedure is harmless and efficient, yet I hesitate to recommend it for two reasons: In the first place, the dilatation of the cervical ring will undoubtedly tend to a relaxation of the entire muscular structure of the uterus as we see it during the ordinary dilatation and curettage for other purposes. If a sound

is introduced into a nonpregnant uterus before dilatation of the cervix and again after this procedure, a difference in the measurements of the cavity is at once apparent. It seems to me that this relaxation can also occur during the prophylactic stretching of the cervix recommended for the relief of nausea and vomiting of early pregnancy, and that unfortunate results may follow. In the second place, the passage of a dilating instrument, unless great care is observed in cleansing the region of the external os, may introduce infectious organisms into the canal itself and if these should pass beyond the level of the internal os, infection of the endometrium or chorion may result, with possible expulsion of the ovum or its death.

Cauterization of Cervical Erosions.—The presence of cervical "erosions," or so-called ulcerations, has been given a place in the etiology of the vomiting in the early months of pregnancy. Whether we can attribute a direct reflex origin to the erosion due to irritation of the nerve endings in the cervix, or whether the presence of such discrepancies in the mucous membrane of the cervix results in a low grade of sepsis from absorption, is undecided. At any rate, the mere finding of such a lesion should lead to its correction, and this can be done in most instances with benefit to the patient. Whether this be by direct effect on the pathological process or for psychic reasons need not be considered. Cauterization of the eroded area with nitrate of silver at intervals of several days, together with the application of a depleting tampon, has never, in my hands, had any deleterious effect in so far as abortion is concerned. Patients experience a great deal of relief from the disagreeable and irritating discharge which usually is associated with this lesion and which becomes worse during pregnancy because of the increased hyperemia of the cervix. Lacerations cannot, of course, be done away with at this time for obvious reasons, but this need not preclude the treatment of the associated erosion, although the effect may only be temporary.

General Hygiene.—Of course the local treatment should go hand in hand with general hygienic measures, including some that are to be directed particularly to the symptoms. In order to treat intelligently a given case we must take into consideration the degree to which the vomiting has progressed. In the milder cases general medical measures often suffice, and these are so well known that it is necessary merely to enumerate them without

going into particular details, although mention may be made of certain therapeutic procedures that are found to produce excellent results. In the first place, the patient must be given a certain amount of rest during the twenty-four hours in addition to the usual sleeping period. As patients are very apt, in mild degrees of this disorder, to experience the nausea on arising, it is advisable to have them take nourishment on awakening and then to go back to bed for another hour at least, lying on the right side if possible, so as to facilitate the emptying of the stomach. This early breakfast should consist of toast, zwieback, and a cup of tea, or the proverbially accepted black coffee.

The patient should be directed to get up an hour or two after this early meal and proceed to dress in a leisurely manner, after which a second breakfast may be taken of whatever she desires. As a rule the nausea which follows this meal disappears within a short time, or, if vomiting does take place, the entire meal may not be evacuated. In many patients there is no further disturbance during the day, but others experience nausea and occasional periods of vomiting at any time during the waking hours. Another rest period, if this can be secured in the middle of the day, is often advantageous. Meals should be taken at regular intervals and it would be better for the usual quantities to be divided so that the patient eats not three, but six or seven, times a day.

In many women the production of saliva seems to have a favorable effect, and such patients may be directed to carry about with them hard sweet crackers, raisins, chocolate, or similar articles to chew at intervals between the regular meals. Chewing gum also seems to be of value at this time. Ordinarily, even if vomiting occurs two or three times during the twenty-four hours, no loss in weight results because at least some of the food is retained and digested. In a more severe grade of this disorder, however, the quantity of vomited material varies from one half to the entire amount ingested, and, in such cases, unless the process is stopped, starvation with its attending bad effects results. It may be advisable to have such patients remain in bed the greater part of the day in a well-ventilated, quiet room, until a balance in the food requirements has been obtained. In this type of the disease the so-called carbohydrate scheme of dieting as worked out by a number of investigators is of great value.

Diet Schedule.—I have been in the habit of furnishing patients with mild vomiting with a diet schedule as follows: They are directed to avoid all meat, soup, and fats during the period of vomiting and to subsist entirely on cereals, stewed fruits, fresh vegetables and breadstuffs, taking six, rather than the usual three, daily meals. From one to three pints of boiled water in which two or three teaspoonfuls of milk sugar are dissolved must be taken during teach twenty-four-hour period. If there is a complaint of "acid stomach," the patient in addition should take a teaspoonful of bicarbonate of soda in a glassful of water on retiring. Sound sleep is favored by taking a warm bath before retiring.

Corpus Luteum Extract.—If the above directions do not help the condition the patient is to report at once. At this time I have occasionally found the hypodermic injection of corpus luteum extract useful, although I am not prepared to state whether the effect is really due to the drug or to the mental state induced by its administration. At any rate we may credit Dr. J. C. Hirst of Philadelphia with the popularization of a remedy, the results from which seem to give us a fair basis for hope in some cases. As he found that almost 90 per cent of his series of unselected cases were favorably influenced, he may be justified in claiming that the lack of normal corpus luteum absorption is a factor in the nausea of pregnancy, and that therefore it can be relieved by a hypodermic or intramuscular injection of the extract. In the cases in which it has been of benefit, I found that daily injections for a period of a week, or on alternate days for a period of two weeks, seem to give the best results.

An array of specific drugs has been recommended to overcome the nausea of pregnancy, including cerium oxylate, dilute carbolic acid, cocain, bismuth, pepsin, etc., and while in isolated cases they seem to do good, the results are usually unsatisfactory and much time may be lost while trying them out. Since the toxic origin of hyperemesis has been generally admitted, the employment of drugs for the purpose has largely been abandoned.

Laxatives are usually indicated, and it is necessary to prescribe them in pill form to favor retention, although in the severer cases even this is ineffective. The extract of cascara in 5 grain doses alone, or combined with belladonna, tincture of nux vomica or aloes, is the most effective laxative and preferably

should be given on retiring, supplemented by a soapsuds enema in the morning.

The use of the heavier mineral oils which have been so much in vogue during recent years is unsatisfactory in hyperemesis, as the patients demur against the swallowing of such large doses and the results are uncertain. An occasional half-ounce dose of castor oil, if the patient can take it, is valuable and likewise small doses of calamel given in doses of from ¼ to ½ a grain at half-hour intervals until a total of 2 or 3 grains is taken. Unfortunately, calomel must be followed by a saline the next morning, and it is often difficult for patients to swallow such a dose on getting up. In the severer cases, where jaundice is present and possible necrosis of the liver cells, calomel is, of course, contra-indicated.

Prognosis.—It is usually possible with the methods of handling these cases as outlined above, to carry a patient through the early months, and, if her mental condition can be favorably influenced and her patience developed, she can be assured that the vomiting will cease at the expiration of the third, or not later than the fourth, month of her pregnancy. I have seen numerous cases in which this has occurred and the knowledge of the fact has buoyed up many a patient until the end of the period stated. Why the vomiting should cease at the expiration of a time limit is not yet explained, but as a clinical observation it is well attested by numerous cases.

We may assume that in the degree of vomiting referred to there is little or no pathological change in the essential organs of elimination such as the liver and kidneys, but we must be very careful to differentiate these mild cases of vomiting from those which may be called pernicious in which, as described in the section on symptomatology, the patient is unable to retain any food at all, does not respond to the methods of treatment described, loses very rapidly in flesh and strength and may within a short time present an appearance of extreme emaciation. In such cases we are dealing with a very serious condition that may require our utmost efforts to overcome. It is essential to bear in mind that we are dealing with a toxemia due to perverted function and that by our treatment we must satisfy certain well-defined needs, which may be considered in turn.

First and foremost, the patient's nervous system must be put

absolutely at rest. Such women are racked from the constant vomiting, they are weak from the lack of food and irritated by the numerous methods of treatment that have usually been employed. Absolute rest in bed in a dark room to which fresh air can have free access must be insisted upon and the visits of relatives and friends forbidden. The patient should be placed in charge of a capable nurse who is to be made responsible for the absolute carrying out of the physician's directions and under no circumstances must these be interfered with by sympathizing relatives. The administration of sedatives and narcotics may be indicated during this period and for this purpose the hypodermic administration of morphine in ¼-grain doses, together with atropin (1/150 gr.), should be employed to secure the much needed sleep. Chloral hydrate in doses of from 20 to 40 grains, and the mixed bromids in doses of from 30 to 60 grains by rectum in one of the nutrient enemas are also very efficient. The patient must not be allowed to read or to tax her strength in any manner.

The next condition to be fulfilled is to supply the dehydrated tissues with water. The giving of water by mouth is often impossible; in such cases it must be given by rectum, under the skin, or into a vein, depending on the severity of the individual case. The third desideratum is the supplying of nutrients, and as mouth feeding in such patients is impossible, the necessary food must be given by rectum. Fourth, the emunctories must be thoroughly attended to. Warm baths or bed baths for the skin, an open, airy room for the lungs, and irrigations for the bowels, must all be supplied.

Care, Routine of.—A more or less routine plan may be outlined as follows, to be modified as the individual needs of the patient require: A quiet, well-ventilated room which can be darkened, either in the patient's home or, preferably in the hospital, and absolute rest in bed, with no visitors. Beginning in the morning, about eight o'clock, a cleansing enema is given with soapsuds to which glycerin may be added in the proportion of one half an ounce to the quart. After this has been completely evacuated, 8 ounces of a 5 per cent glucose solution to which from 30 to 60 grains of bicarbonate of soda have been added, is given by rectum. This rectal infusion is repeated at twelve, four, and eight o'clock, a total of four doses with 32 ounces of fluid and from 2 to 4 drams of bicarbonate of soda. If the skin is dry and does not seem to

function well, a hot pack lasting from ten to twenty minutes may be given after the eight P. M. rectal infusion. This will usually insure the distribution of the circulating blood under the skin, bring about perspiration, make the body desirous of more fluid, and induce a quiet sleep. Nothing whatever is given by mouth until the vomiting begins to lessen, when small doses of hot water or weak lemonade may be taken, together with a mouthful or two of cracker or toast. The teeth should be kept clean and the tongue scraped, as this contributes very much to the comfort of the patient. The injection of fluid by rectum may usually be kept up for several days without producing any irritation, but if the rectum becomes irritated the addition of 20 drops of camphorated tincture of opium to each glucose instillation will obviate this difficulty and, moreover, act as a sedative. If the patient is restless and cannot sleep, 15 grains of chloral or 30 grains of sodium bromid may be introduced into the evening glucose instillation.

The urine of these patients often shows marked traces of albumin, diacetic acid and oxybutyric acid; it is dark in color, concentrated and of high specific gravity. It is on this account that the alkali is given and we may continue it in doses sufficiently large to produce an alkaline reaction in the urine. I have found, however, that more than 60 grains of soda bicarbonate by rectum may prove irritating and in its place a pint or more of Kalak water may be used, or one and one-half ounces of milk of magnesia. Salt solution must under no consideration be employed, as the excretion of the salt contents through the kidneys only increases the renal irritability or the nephritis which may already be present. In cases in which dehydration of the body is more advanced and in which the acidosis is not cleared up within a day or two, the subcutaneous injection of sterile decinormal soda bicarbonate solution under the breasts may be employed, or a solution of glucose may be injected intravenously, which in some instances has been recommended as strong as 25 per cent. In my own experience I have hesitated to use this stronger and more viscid solution and believe that equally good results will be obtained from a 5 per cent solution. Even in extreme cases of emaciation, glucose may be given intravenously and I have seen excellent results in patients in whom 8 ounces were given daily for two or three days in succession. A

more detailed reference to use of glucose infusions will be found later on in this chapter.

Thirst, Relief of.—Women who complain bitterly of the thirst and yet vomit as soon as any water is taken will be relieved of this distressing condition within twenty-four hours after the instillation of the fluid by rectum has been begun. It is unnecessary to employ any drug administration at this time, although the use of the corpus luteum extract by intramuscular injection may be resorted to. If used in the severe cases it should be given at least twice daily to obtain any possible favorable effect.

It will be noted that in the above method of treating hyperemesis no attempt is made to introduce nutrient materials in the enemas such as have been so generally used for the purpose, including eggs, peptonized milk, beef extracts, etc. It seems to me sufficiently well demonstrated that the rectum fails to absorb any such materials even in health, and their administration in an emaciated patient can certainly be of no avail. I believe, moreover, that the absorptive function of the rectal mucosa is interfered with by the introduction of these materials and that the necessary ingestion of water is thus prevented. I have given up such methods entirely and believe better results follow the use of water alone without any of the nutrient substances formerly so much in vogue.

Induction of Abortion—When Advisable.—Although a considerable number of cases are improved by this treatment, it must not be persisted in if the patient fails to show any change for the better within a few days, and if the acidosis, as shown by daily urine examinations, does not improve; if vomiting of bile-stained fluid or coffee-ground material occurs; if the yellow staining of the skin and sclera persists or grows deeper; if the blood-pressure falls day by day; if the urine becomes less in amount and of a greater specific gravity—all temporizing methods should be stopped and the uterus emptied. Too many women are carried along from day to day in the hope that one or the other method of treatment will pull them through and then, when an abortion is finally attempted, the patient is too weak to survive its effects.

We can always feel that the induction of abortion is justified in such cases because, if the woman recovers, she may usually be guided through another pregnancy with proper care. I have had

a personal experience with several patients who, when pregnant for the first time, developed a hyperemesis which grew rapidly worse notwithstanding all treatment, in whom a rapid recovery followed the emptying of the uterus and in their next attempt at a pregnancy no harmful consequences whatever followed. The induction of abortion should therefore not be delayed beyond the limits referred to above, and when done it must be carried out under the most careful auspices. This is essential because a degree of infection which would not affect an ordinary, healthy woman might prove fatal in a case of this kind.

Methods of Abortion.—As little shock as possible must be produced in the abortion, and it is therefore advisable to precede the clear-

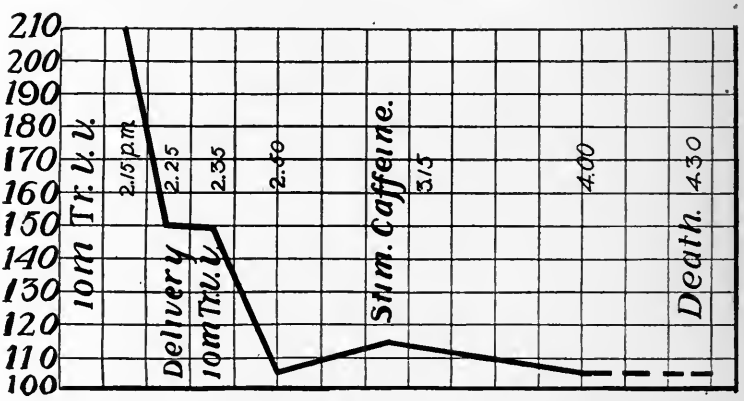

Fig. 23.—Blood-pressure Chart from a Case of Eclampsia in Which Rapid Delivery Was Done and Veratrum Viride Was Given. Shows a fall of 105 millimeter in thir-yfive minutes (Bailey).

ing out of the uterus, especially if we are dealing with a primipara, by a preliminary packing of the cervix for twenty-four hours with a narrow strip of gauze. This softens up the cervix, can be done without anesthesia and makes the instrumental dilatation twenty-four hours later very much easier. In pregnancies which have reached the third month the membranes may also be ruptured, as this at once relieves intra-uterine tension and tends to spontaneous abortion. It is not unusual to find when the gauze is removed that the cervix, even in primiparae, is so softened and dilated that the ovum projects from it. The patient is prepared as for dilatation and curettage twenty-four hours after the initial introduction of gauze. The operation can usually be done under gas-oxygen anesthesia preceded by a hypodermic of ¼ of a grain of morphin.

Chloroform is absolutely contra-indicated on account of its effect on the liver; and ether, while less dangerous, is unnecessary, requires more time for administration and may produce a deleterious effect on the kidneys (Figs. 23, 24, 25). With the patient in the lithotomy position, or better still, with the legs held by two assistants, the vulva is quickly shaved if this has not been done before the packing is introduced, and the surrounding skin surfaces and the

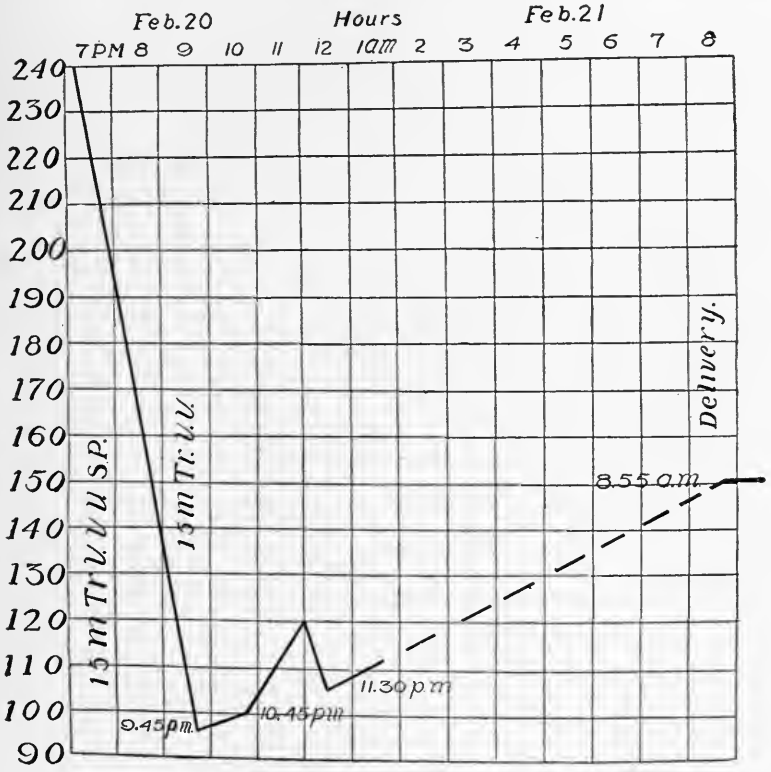

FIG. 24.—BLOOD-PRESSURE CHART FROM A PRE-ECLAMPTIC CASE, SHOWING RAPID FALL (145 MILLIMETER WITHIN THREE HOURS) AFTER THE ADMINISTRATION OF VERATRUM VIRIDE ALONE (Bailey).

vagina painted with a 3½ per cent tincture of iodin. The cervix is then exposed through a speculum, seized with a double tenaculum forceps, and, if the dilatation is insufficient, it may be completed with the graduated sounds. A branched dilator is not advisable because of the possibility of tearing the softened cervix. In fact, a more complete and satisfactory dilatation is possible with the Hegar or a similar instrument. The fruit-sac can usually

be seized with an ordinary Foster's sponge-holder and removed. If it does not come away in its entirety, the clearing out of the uterine cavity should be readily and quickly done with a sponge-holder, or with a large and not very sharp curet, after which the cavity is wiped dry with gauze and packed with a strip of plain gauze one inch wide. Such patients do not stand the loss of blood well and it is desirable, therefore, to extract as much of the ovum in one piece as possible. The bleeding can also be reduced by a hypodermic injection of 1 cubic centimeter of pituitrin just before the dilatation is begun, which controls the bleeding during the operation and the gauze pack exercises a similar function immediately afterwards.

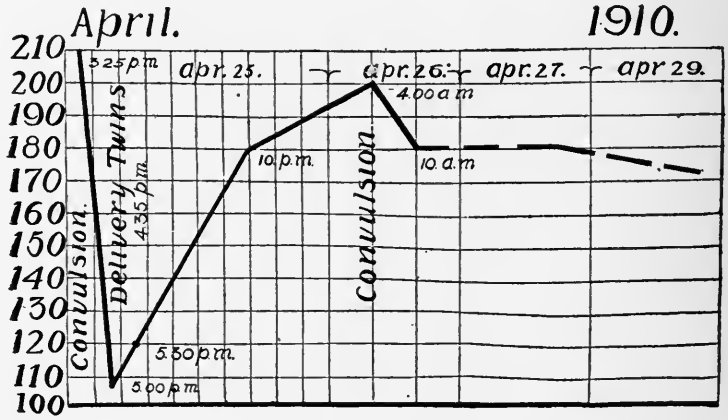

FIG. 25.—BLOOD-PRESSURE CHART FROM A CASE OF ECLAMPSIA WITH TWINS, SHOWING TEMPORARY REDUCTION AFTER DELIVERY BUT WITH FINAL RECOVERY (Bailey).

VAGINAL HYSTEROTOMY IN PRIMIPARÆ.—In primiparæ with long, rigid cervices, in which dilatation would ordinarily be a slow process, and who are in bad general condition from exhaustion, a rapid and satisfactory emptying of the uterus may be done by a vaginal hysterotomy, particularly if the pregnancy has reached the third month. In such cases the preliminary gauze pack is not needed. The patient is prepared, anesthetized with gas-oxygen followed by a small amount of ether; the cervix is seized and pulled down and a transverse incision made at the bladder junction in the anterior vaginal vault. It is usually not necessary to strip back the bladder very far. The anterior lip of the cervix is then cut through in the median line to the level of the internal os, which gives sufficient room for the evacuation of the fruit-sac.

The cervical incision is then quickly closed with several interrupted chromic gut sutures, followed by suture of the mucous membrane wound in the vaginal fornix. The uterine cavity, including the vagina, is firmly packed with narrow strip (from ¼ to ½ inch) of iodoformized or plain gauze. If the fruit-sac cannot be removed in its entirety, a rapid curetting of the uterine cavity may be done. The packing is essential to stop the bleeding from the uterus or the operative wounds, as the patient needs to conserve every drop of blood at this time.

Shock.—Shock is common in these cases, but may usually be avoided by instituting the rectal glucose feedings (8 ounces of a 5 per cent solution) every four hours as soon as the patient is returned to bed. I have found it advisable to keep up the glucose infusions for five days or more in lessened amounts. When the patient is greatly emaciated a hypodermoclysis of a pint of 5 per cent sugar solution may be given under each breast, or 8 ounces of the solution carefully sterilized, may be injected intravenously. When shock is marked the intravenous injection of a stronger glucose solution (25 per cent) to which gum acacia has been added, as recommended by Farrar, is of great value and I have employed it with excellent results in several cases.

Before an operative procedure in a toxic patient, whether in the early or late months of pregnancy, the acidosis which is usually present must be combated by the administration of an alkali, preferably sodium bicarbonate. According to Palmer and Van Slyke, 0.5 grain of the latter for each forty-two pounds of body weight will raise the carbon dioxid combining power of the blood 1 per cent by volume. Killian recommends its administration intravenously in a 4 per cent solution, which can be given before operation and then continued by rectal infusions until recovery takes place.

The lowered blood-pressure which is usually found must be combated by the administrated of adrenalin in doses of from 10 to 20 minims by hypodermic, or 40 minims may be included in the glucose rectal infusion. The body heat must also be conserved and chilling of the patient avoided during operation and immediately afterwards. In a great many cases death results within twenty-four hours, or later, due not only to the extreme degree of shock and exhaustion, but to the development of various contributory causes—

pneumonia, embolism, infection—all of which are, of course, to be treated symptomatically.

Hospital Care.—The treatment of hyperemesis of pregnancy outlined here must be varied not only to suit the individual case but must also be adapted to the surroundings under which it has to be carried out. In private homes the necessary isolation and quiet is often difficult to obtain, and unless this can be satisfactorily done, it is better to send the patient to a hospital. The milder grades of the disturbance can usually be managed without recourse to hospital discipline, but as soon as the vomiting becomes to any degree extreme and uncontrollable, a transfer to the hospital is not only desirable but necessary. The change from bad to worse may take place very rapidly, and, as a general rule, the emptying of the uterus cannot be as safely done in the home as under proper hospital surroundings.

Supplementary Measures.—The scheme of treatment for pernicious vomiting as described in the preceding paragraphs may be supplemented by recourse to a variety of other measures which are reported in the literature on the subject. I do not propose to include the various preparations and drugs recommended merely for the specific purpose of correcting nausea or vomiting, for their use is more or less empirical and without regard, in most instances, to any possible underlying etiological factor. It would be impossible, in fact, to enumerate them in the limits of these pages and no good purpose would be served. We may, however, refer briefly to certain measures for the relief of this condition which, to some extent, have a rational basis for their use.

Sera and Gland Extracts.—*Normal Human Blood Serum.*—The assumption that the toxemia which underlies excessive vomiting is due to circulating materials in the blood of the patient, which are either not present in nonpregnant individuals or may be rendered inert by the blood of the latter, has led to the employment of normal human blood serum by several investigators. Thus Fieux was probably the first to suggest these injections and Bondy, somewhat later, presented his observations on 21 cases of hyperemesis. He was led to use serum after studying the findings from the Abderhalden tests, according to which it is assumed that, shortly after conception takes place, substances circulate in the maternal organism which may be regarded as foreign matter. Under certain circumstances, not yet determined, these substances can

upset the perfect balance of the organism and thus produce vomiting among other symptoms. The activity of these substances in the organism is to be traced either to their increased formation or to the diminished combination with antidotes, resulting in a condition of toxemia, and their effect may subsequently be increased by psychic influences, neuropathic disposition or pathological processes in the genital organs themselves. The dosage in these cases is from 10 to 15 cubic centimeters of serum from a normal, pregnant woman with a negative Wassermann, by injection into the back muscles one or more times daily.

Horse serum and Ringer's solution have also been employed for hyperemesis with reports of a similar effect.

Negative Results.—Among the negative results reported we find an observation by Rubeska in two cases. In the first case, 10 cubic centimeters of normal pregnancy serum was injected into the gluteal region, and this amount was given three times on the next day but without result, so that abortion was required. In the second case, 40 cubic centimeters were given into the median basilic vein and two days later an equal quantity in another vein, together with 20 cubic centimeters subcutaneously. Vomiting seemed to be slightly improved for a short time, but on becoming worse the next day another injection of 55 cubic centimeters was given into the vein and 15 cubic centimeters intramuscularly. No result was obtained and abortion had to be induced. J. Whitridge Williams states that he has also been unable to confirm the claims advanced for these serum injections and believes that any good results which followed may be attributed to suggestion.

Fetal Serum.—During the course of an investigation on the effect of fetal serum on the onset of labor, Rongy observed a favorable effect in a patient with well marked symptoms of impending eclampsia. By analogy serum from the cord blood was used in four severe vomiting cases with apparently favorable results. From 10 to 15 cubic centimeters were given intramuscularly at intervals of several days and in one rather severe case it was given into a vein. In all these patients the vomiting finally ceased, but the severity of the symptoms as described by the author makes one hesitate about resorting to the procedure at the expense of valuable time lost in emptying the uterus.

Placental Extracts.—From the use of fetal serum it seems but a step to the employment of the placental extract and we find this pro-

cedure advocated by Cary, who bases the administration of this substance on certain animal experiments made by A. H. Curtis. The latter found that injections of placental extracts in rabbits and guinea pigs increased the resistance from immunity to such an extent that the existing balance was altered, causing death and lysis. Cary then reasoned that if toxemia of early pregnancy is due to a lowered immunity to the growth of the syncytium, the placenta may stimulate by acting as an antigen. Moreover, if the proteolytic ferment is lower than normal, as demonstrated by the negative Abderhalden reaction, the desiccated placenta may increase the ferment content of the blood. Finally, if the placenta is an internal secretory gland, its administration may increase the activity of the thyroid and adrenals and thus hasten the oxidation of partial protein by throwing split products into the circulation.

Cary treated 13 cases of vomiting at different periods of gestation with the placental extract. Of the 13, 7 stopped vomiting within a day or two and the nausea soon disappeared; 2 improved and remained fairly free from nausea; in 2 the results were not satisfactory; the other 2 were lost sight of. In a series of 6 cases treated by an associate, 3 showed good results with varying success in the other 3. The placental extract was given by mouth in 5-grain capsules three times daily, over a period of from ten to twelve days. In one of the series, a woman with pre-eclamptic toxemia, a stillbirth resulted, although the toxic symptoms of the mother became no worse during the administration of the extract and the blood-pressure fell about twenty points.

In connection with this theory, attention must be called to the fact that, in so far as cellular activity is concerned, the placenta is merely active during the stage of trophoblastic development which is the only time during which a hormone or other secretory material is formed. A placental extract desired for therapeutic purposes should, according to Culbertson, be prepared from early placenta or early chorionic villi, which, in the human female, would have to be before the fourth month. It has been shown experimentally that the physiological action of the trophoblast is identical with that of the corpus luteum of pregnancy, which may explain the favorable effects claimed for the latter when administered for the relief of hyperemesis. Unfortunately, hormones do not produce antibodies and cannot be demonstrated by any complement fixation tests. The entire subject is surrounded by so many uncertainties that further obser-

vations are demanded before any recommendations can be made.

Adrenalin Chlorid.—Adrenal insufficiency as a factor in the production of the vomiting of pregnancy was first advanced by Rebaudi and has since been discussed by others. Zuloaga declares that such adrenal insufficiency can be diagnosed by the fact that a persistent white line in the skin follows the drawing of the finger nail over the skin. This white line disappears during treatment. A solution of adrenalin chlorid (1 : 1000) may be given well diluted by mouth in doses of 20 drops three times daily, or by rectum in double this amount in the nutrient enemata. In severe cases hypodermics of from 5 to 10 minims are indicated. The most recent report is by Rathery and Bordet, who arrested at once a serious vomiting by the injection of 250 cubic centimeters of normal salt solution containing 10 drops of "epinephrin," repeated daily up to a total of 2.5 milligrams. The procedure is worthy of further trial.

Nasopharyngeal Complications.—The association between the genitals and the nasal and pharyngeal mucous membranes, as manifested by congestion of the latter during the menstrual period and the reported relief of dysmenorrhea by applications of cocain to certain areas in the nose, has directed attention to the possible effect on hyperemesis of similar procedures. Nausea and retching on rising in the morning provoked by a nasopharyngeal catarrh with the presence of tenacious mucus, must be treated by alkaline gargles and the application of a 5 or 10 per cent solution of nitrate of silver to the affected area. If examination of the nasal passages shows a red, congested turbinate region, local applications of a 2 per cent cocain muriate solution or adrenalin (1 :1000) often give remarkably good results.

Sedative Drugs.—The use of sedative drugs in hyperemesis has been largely recommended by those who insist that a "nervous habit" accounts for many cases of moderate severity, and that the act of vomiting is simply a response to the feeling of nausea. In addition to dietetic regulations and a sojourn in a hospital, Lynch, for example, advises keeping the patient under the constant influence of large doses of bromid by rectum, beginning with doses of from 40 to 60 grains every four hours, and continuing until cessation of the vomiting.

Opium.—The rectal administration of powdered opium in suppositories of from 1 to 2 grains at four-hour intervals, has occa-

sionally given me good results, also in asthenic, tired-out women, the hypodermic use of ⅛ grain of morphin every three or four hours, or 1 grain of codein at similar intervals. The employment of other narcotics and hypnotics, including trional, sulphonal, etc., has not been satisfactory. But a period of rest secured by opiates often tides the patient over a time during which eliminatory and feeding measures may help to restore a balance.

Ipecac.—It is usually assumed that excessive vomiting produces a condition of the mucous membrane of the stomach akin to gastritis, that is, one of extreme congestion. This is probably true, but if there is marked nausea without much vomiting, the circulation of the stomach is likely to be poor and its activity depressed. In this condition ipecac has been shown to be of value; drop doses of the wine in a teaspoonful of water at half-hour intervals having been found very efficient. Care must be taken to exclude cases of actual gastritis, as the nausea or vomiting from the latter will be rendered worse by this drug.

Cocain, Menthol, Etc.—The administration of cocain, menthol, peppermint, and similar preparations for their sedative effect on the gastric mucosa has not given me any good results, nor has the use of pure carbolic in minim doses well diluted. Cocain muriate in doses of ⅛ grain with a small quantity of water given before eating will occasionally favor the retention of food, but its effects are very uncertain. The subcarbonate of bismuth in 10-grain doses given in water seems to have a better effect.

Blood Transfusion.—The indications for the injection of human blood have also been extended to include the toxemias of pregnancy, both in the early and late months. Thus, Keator reports a case in which severe hyperemesis in the third month of pregnancy was associated with purpuric skin areas, nose bleed, and jaundice. The condition did not respond to treatment and the uterus was emptied. Hemorrhages from various places continued, however, and the clotting time of the blood was over ten minutes. The undoubted hemophilia, although no previous history of earlier attacks was obtainable, prompted blood transfusion by the direct artery to vein method. Collapse resulted, but the patient finally made a good recovery. The occasional appearance of purpuric spots and mucous membrane hemorrhages in severe cases of hyperemesis furnishes, it seems to me, a good indication for blood transfusion.

ACUTE YELLOW ATROPHY OF LIVER

Unfortunately little can be said of the treatment of acute yellow atrophy of the liver. As soon as the diagnosis has been determined, immediate emptying of the uterus is indicated, although some successful case reports are on hand in which temporizing measures were resorted to. The operation must be performed with a minimum of shock, as already described, and the after-care of the case requires the utmost skill and patience. The prognosis is unfortunately so bad that nothing can be done in the majority of these cases.

NEPHRITIS AND ECLAMPSIA

The treatment of nephritic and preëclamptic toxemia need not be discussed separately but can be considered with that of eclampsia. The appearance in pregnancy of the symptoms noted in a previous chapter under this head should always call for prophylactic measures. If the diagnosis of a preëclamptic condition has been made, careful and frequently repeated urinalyses are essential and the amount of albumin should be carefully watched by means of an Esbach tube. The ordinary boiling and ring tests are insufficient. When from ¾ to 1 gram of albumin per liter is present, the diet should at once be restricted to milk, cereals and toast, with as much water as possible. The patient should be put to bed and kept quiet. The so-called "imperial drink" (cream of tartar, 1 teaspoonful, juice of half a lemon, water, 1 pint, with sugar to flavor) is a very agreeable beverage and also slightly diuretic. At least thirty to forty ounces of urine should be passed by the patient every twenty-four hours. The skin must be kept functionating with daily warm baths, and a saline purge (magnesium sulphate) at regular intervals is necessary.

The blood-pressure should be carefully watched and if it persists between 180 to 200, palliative treatment should be supplemented by more radical measures, especially if the albuminuria goes up to 5 grams or more per liter. Hot packs, arterial dilators (chloral in doses of from 5 to 10 grains every four hours) and colonic irrigations may again be tried, but preparations for the induction of labor should

always be made. The abstraction of a pint or more of blood in otherwise vigorous and well-nourished patients may be resorted to, but I am not inclined to favor this procedure because, whatever method of delivery is finally employed, may result in such considerable blood loss that marked shock results. If a woman's condition is so serious as to require venesection, it is usually grave enough to call for the emptying of the uterus.

Eclampsia, Treatment of.—In beginning the discussion of the treatment of the final group in our classification, it may be noted that during the last quarter of a century the treatment of eclampsia, using this term in its broader sense, has vacillated between two extreme views and even at the present time there are many adherents in each camp, although the number of those who favor a middle ground is constantly increasing. During the period when the eclamptic woman was supposed to be suffering from a functional kidney disorder and immediate relief was believed to consist in bleeding, a great deal of harm was done because the cases were not selected. Stout women bore bleeding well and often recovered, but the thin, frail type usually succumbed or underwent a prolonged convalescence. After it was recognized that the fetus itself might be the exciting cause of the symptoms, immediate emptying the uterus was advocated and the forcible dilatation of the cerxix uteri with mechanical dilators, such as the Bossi, was widely practiced. As the result of these methods of *accouchement forcé,* the lower genital tract was subjected usually to extensive lacerations with excessive shock, loss of blood, and frequent sepsis, together with more or less permanent mutilation of the parts.

It was soon admitted that such methods were contrary to the best interests of the patient, and, where the idea of immediate delivery still persisted, more skillful methods were called into play, including the Dührseen incisions, the vaginal cesarean section, and later the abdominal variety of this operation. At the same time we find Stroganoff and his adherents endeavoring to enforce their ideas, based on very conservative methods, in which little attention was paid to the fetus *in utero,* but every means was taken to reduce the process of toxin formation in the mother and to overcome its irritating effects by the administration of morphin and other sedative drugs.

Besides the conservative Stroganoff procedure, venesection and methods of delivery characterized by less radical procedures, such as the introduction of bougies, vaginal packs and the dilating

bags, are now more widely employed, but we are still unfortunately groping for a method of treatment that will meet more specific indications. In the present state of our knowledge, however, it is just as well that we refrain from innovations in treatment, and select those procedures in which experience has shown the lowest possible mortality, both for the mother and child, and a minimum of subsequent injury to the mother. In view of our ignorance of the etiology of eclampsia it would be unfair to recommend any one method of treatment. Each individual case should be thoroughly studied and the procedures selected which are best adapted to the surroundings of the patient on the one hand, and the skill of the attendant on the other. This seems much more sensible than to claim that all cases coming under observation must be handled according to a routine procedure. In other words, as I have repeatedly stated, the patient, and not the disease, is to be treated.

Prophylactic Measures.—The simplest conception of the treatment of this disturbance includes first, the management of the so-called preëclamptic stage; second, that of the series of phenomena to which the term "true eclampsia" is usually applied. Before proceeding, however, to the discussion of the manner of dealing with the preëclamptic stage, described in a general way in the preceding section, we must take into consideration the prophylactic handling of these patients, as soon as any warnings of a disturbance in the body metabolism become evident. It is generally assumed that, under ordinary circumstances, in a pregnant woman in good general health, with emunctories in working order, no particular danger from this source exists. It is unwise, however, to agree with this complete optimism. Pregnant women, even if apparently well, should be looked upon as being in an extremely unstable condition in regard to their metabolism and subject to very sudden deviations in the normal bodily functions. It is therefore advisable for the attending physician in every case of pregnancy to warn the patient of what may occur in the way of symptoms that in time might lead to an eclamptic seizure.

Preventive measures in the preëclamptic stage are simply those recognized as essential in the ordinary hygiene of pregnancy, that is, good food, plenty of fresh air, moderate exercise, attention to the emunctories, peace of mind and freedom from

care and worry. When these can be provided a great part of the battle against abnormal deviations is already won. It is not necessary to pursue this phase of the subject further, as it has been amply treated elsewhere. It is well, however, to mention here the deviations from the normal upon which to base our estimate as to whether the patient's physiology is fulfilling the calls made upon it. First and foremost, every pregnant woman should be seen at regular intervals by her chosen attending physician, at which times she must bring a part of the twenty-four-hour urine specimen for examination. Patients should also be urged to note any unusual occurrences during the interval since the last visit and be ready to consult their physician with reference to the same. The visits should be made at no greater than monthly intervals and if abnormalities are present more frequent visits are necessary.

The patient should be carefully questioned at the office visit about the condition of her bowels, frequency of urination, headaches, digestive disturbances, pain, visual abnormalities, etc. Not every patient presenting deviations from the normal in the symptoms referred to is necessarily in the preëclamptic stage. Headaches may be due to other causes, and if unassociated with albuminuria or other urinary abnormalities, edema, or visual disturbances, they may be treated in the accepted manner. The intestinal tract is at fault in a great many cases as well as the eyes; and if headaches persist, notwithstanding attention to the correction of digestive disturbances, and if accompanied with irregular vision, it is advisable to have the patient consult an ophthalmologist. The correction of visual disturbances, which may not have been present before pregnancy, or at least not in an annoying form, should be urged upon the patient, and in a great many instances it will be found that the wearing of glasses relieves headaches that were considered a symptom of the preeclamptic stage.

Although we accept pain in the pit of the stomach as a forewarning of an eclamptic seizure, this is not true in every case. Hyperacidity is a frequent accompaniment of pregnancy, and in some cases the resulting distress after eating is not only annoying but may alarm the patient and also her attending physician. If present, as it so frequently is during the later months of pregnancy, it should be alleviated by the administration of alkalis,

such as soda bicarbonate, milk of magnesia, aromatic spirits of ammonia, etc. I have had good results from dilute hydrochloric acid in ten-drop doses three times daily after meals. Patients who are afflicted with indigestion and take large amounts of bicarbonate of soda for relief often suffer general abdominal cramplike pains which cease when the drug is stopped. It is not advisable to continue any one alkali for a prolonged period.

Constipation.—The constipation which is such a frequent and annoying symptom in the latter months of pregnancy must be combated in every case, because we may safely assume that it is an underlying factor in the production of many toxemias. Advice on the relief of constipation has taken so many turns that it would be a difficult matter to present it in its entirety. The regulation of the diet, however, so as to include a minimum of meat, soup, cocoa, tea, white bread and similar articles, is essential no matter what form of drug catharsis is employed. The response to treatment varies with the individual, but in any case purging is contraindicated. The regular administration of fluid extract of cascara in doses of from 15 to 30 minims with 1 or 2 drachms of rhubarb and soda mixture is usually effective. The stronger vegetable cathartic pills should be avoided, especially those containing an admixture of aloes. The use of heavy mineral oils has been widely advocated, but the response depends on the individual patient. In some cases the administration of an ounce or two of petroleum oil at bedtime, together with a mild cathartic, has proved very efficacious, but in others absolutely no result is obtained. The oil, to be efficient, must be taken over a long period and is rarely effective unless combined with a cathartic.

Phenolphthalein has also been recommended as an ideal laxative in pregnancy. Its use, however, cannot be long continued, because of its irritating effect on the kidneys. While frequent water drinking has a good effect in favoring bowel action, the hard water from commonly found artesian well supply is productive of an opposite effect. When the water is known to be hard it should be boiled before use and thoroughly aërated. Resort to enemas may be necessary and I have rarely seen any bad effects from them in women who had a great deal of difficulty in securing proper bowel action, even with the assistance of cathartics. Given in the form of a pint of hot soap suds with the patient lying on her left side and repeated if the first injection is

ineffective, enemas need not, in my opinion, become a habit-forming procedure.

Organs of Elimination, Care of.—The necessity of maintaining proper excretion through the medium of the skin and kidneys is obvious and can best be secured by the free drinking of water and by bathing. A warm bath every day or two in the evening on retiring is indicated during pregnancy, but I do not approve of the cold showers on arising in which some women indulge. I believe that the chilling of the body which results is unfavorable and may even be a source of danger. However, those patients who have become accustomed to cold showers may resent their prohibition at this time, but they should be warned against them.

The amount of urine excreted during twenty-four hours should reach at least two or three pints and I often direct patients actually to measure the urine once a week, noting at the same time the color and odor. I consider a reduction in the quantity of urine with an increase in the specific gravity a sign always to be taken note of. Patients are very apt to drink freely of water the day before coming to the doctor's office so as to be provided with a proper specimen. They should therefore be instructed that normal urinary conditions must be insisted upon at all times.

These more or less simple prophylactic measures may be sufficient in most cases to preserve the woman's normal metabolism under ordinary circumstances. There is a certain group of cases, however, in which mild toxic states are present, characterized by frontal headache, torpor, reduction in urinary output, etc., that calls for somewhat more vigorous treatment. A patient who presents herself with this train of symptoms must be cautioned against the gravity of her condition, without, of course, frightening her. It is better to err on the safe side even if the restrictions imposed on the patient seem onerous. The protein foods in such cases should be immediately reduced and a diet of milk and cereals prescribed, together with mild catharsis until improvement results.

The ordinary examination of the urine may not show anything more than a mere trace of albumin and perhaps increased specific gravity, but tests for indican and diacetic acid should always be made. The so-called clearing-out process in such patients must not, however, be overdone. The administration of large doses of calomel and salts is not necessary. In fact, calomel

and salts should not be given to the delicate type of woman, but reserved rather for those who are well-nourished, who present a florid complexion, and who are inclined to stoutness. In the latter 2 grains of calomel in divided doses during the afternoon are to be followed by a tablespoonful of Epsom or similar salts in hot water the next morning and an enema a few hours later. This dose may be repeated at intervals of from five to ten days; otherwise, somewhat larger doses of cascara than the patient has been accustomed to, or small doses of castor oil (½ ounce at bedtime), are valuable. As a general rule, the symptoms will subside under these restrictions, but a patient should be instructed to report at once to her physician if no improvement results, or if the symptoms become worse.

Blood-pressure. — Blood-pressure observations should, of course, be taken, but in many cases we do not find any rise of blood-pressure associated with the group of cases described in the preceding paragraph. The subject of blood-pressure observations and their significance has already been referred to in another chapter. The apparatus for such observations gives very trustworthy information, but it must be used intelligently and with due consideration to the patient. Small, asthenic, poorly nourished individuals may show low blood-pressure, although suffering from moderate degrees of toxemia; whereas the stout, well-nourished patient with a high blood-pressure may so mislead the physician that he believes an eclamptic seizure imminent. Such observations must always be taken into consideration with the urinary findings and the other symptoms. Women who present moderate and continuous elevations of blood-pressure in association with the train of symptoms already referred to may be given arterial dilators if the dietetic and cathartic measures do not produce a result. For instance, a full-blooded patient in her third or fourth pregnancy, who is running a diastolic pressure of 150 millimeters or more, who complains of congestive headaches, and who has a flushed appearance and a full pulse, may take chloral hydrate in 5-grain doses three or four times daily with advantage for periods of four or five days, combined with rest in bed. Relief from headache and nervousness is usually noted within a day or so. As soon as the blood-pressure falls twenty points or more the administration of the drug should cease.

The use of nitroglycerin in stout patients with high blood-

pressure has not been effective in my experience. Unless we can give nitroglycerin in comparatively large doses and know that the preparation is fresh, or unless we can use the spiritus glonoin, the administration of this arterial dilator is of no value. Moreover, the mouth administration of the drug is practically without result, and I have had results only if administered hypodermically. There is no indication whatever for giving veratrum viride at this time. Rest in bed is a very important factor in the more rapid recovery of these patients, and it may be necessary in some instances to remove them from unsatisfactory surroundings to a hospital, where improvement in their condition is usually noted immediately.

Visual Disturbances.—Patients who present the train of symptoms which includes headache, malaise, digestive disturbances, coated tongue, and occasional attacks of dizziness, must be kept under the most careful observation, for at any moment the picture may grow suddenly worse. In most instances, however, sufficient warning is given through the medium of the visual apparatus, and should be heeded immediately. The attending physician should always take note of photophobia, diplopia and other ocular abnormalities, for their appearance demands the most careful attention. Keeping the patient in a darkened room is very helpful in reducing the irritability of the eyes. It is advisable whenever possible to have an examination of the eye-grounds made by an ophthalmologist. The latter can detect retinal changes in which more vigorous action may be indicated. As I have already stated in the description of the pathology of eclampsia, the eye symptoms associated with this condition may prove extremely serious. The presence of retinal hemorrhages or the picture designated as albuminuric retinitis, even if not associated with transitory or permanent blindness, always, in my opinion, calls for the emptying of the uterus. I do not believe that a policy of hesitancy should prevail in these cases in view of the known fact that permanent damage to the eyes may result, even if the acute toxic condition ends in recovery, and that more serious intracranial lesions may be in process of development.

Convulsions.—In another group of cases in which the presence of convulsions is the distinguishing characteristic, opinions differ widely as to the proper treatment. For many years the pendulum has swung from extreme conservatism to extreme radicalism and

back again, and at the present time there is by no means accord as to the proper procedure. It seems to me that here, as under other circumstances, recourse to a middle ground is most essential, and the careful study of the individual patient should be the guiding feature rather than adherence to any routine method of procedure. It may be granted that in a given case the doing away with the convulsions is the essential feature in the treatment. Assuming that the muscular spasms are due to cortical irritation, they may be most satisfactorily subdued by the administration of sedative drugs, which has found expression in the extensive employment of the so-called Stroganoff method, which treats only this symptom, and after the patient is narcotized the natural termination of the labor is awaited. Its advocates bring forward a large series of cases thus treated with exceedingly good results. It must be admitted, however, that the emptying of the uterus is often followed by a cessation of the convulsions and an improvement of the patient in most cases. For this reason it would appear better as a general procedure to adopt the favorable features of both methods of treatment.

Perhaps the description of the treatment of an ordinary case of eclamptic convulsions will explain this more satisfactorily. What shall be done in a given case in which the physician finds that the patient has had one or more general convulsive seizures with a typical clinical picture that leads to the diagnosis of a true eclampsia? First and foremost, the decision should be made to refer the patient to a hospital whenever possible, but in the meantime it is necessary to reduce the possibility of further convulsions and this can be most simply and satisfactorily secured by the proper administration of opium. Thus ¼ of a grain of morphin sulphate with 1/150 of atropin sulphate may be given by hypodermic immediately, to be repeated at intervals of one, two, or three hours, depending on the severity of the seizure. Meanwhile preparations can be made for the transfer of the patient. No one need hesitate to administer morphin in such cases until the full and complete physiological result is secured, as evidenced by the fall of the respirations to sixteen or even to fourteen per minute. Atropin may be objected to as an accompaniment because of its well known desiccating effect on the secretions, but its value in overcoming certain undesirable effects of the opium more than compensates for any possible physiological effect of its own. Moreover, atropin is a relaxant of muscular tissue, especially of

the unstriped variety and reduces the tendency to pulmonary edema.

Examinations, Vaginal and Rectal.—No attempt should be made to examine a patient in eclampsia until she has become thoroughly narcotized, because such an examination may be sufficient to set up further convulsive spasms. Chloroform should never be employed to secure the necessary relaxation, but ether may be used with less danger. The tongue must be protected against injury by inserting a wedge of wood (a clothespin, the handle of a hairbrush, or a spoon) between the molar teeth, to be retained in place during the convulsive seizure and reïnserted as needed. I would suggest omitting the vaginal examination in such patients unless the vulva can be shaved and properly cleansed because we know that the resistance to general infection in these women is very greatly lowered. A rectal examination is perhaps preferable at this time. If it is found that the cervix is dilated three fingers or more, the membranes may be ruptured and this relief from intra-abdominal tension often has a favorable effect in stopping the convulsions.

Enemas and Stomach Washing.—By this time the family of the patient should have arrived at a decision as to the transfer to a hospital, and where this is possible the further steps in the treatment can be continued in the institution. It may be necessary, however, to carry out further treatment at home. The bowels should be washed out with an enema of hot soap suds as soon as the morphin has become effective. It is advisable to wash the stomach, but unless a stomach tube can be skillfully introduced it is better to omit this procedure, as the introduction may induce further convulsions, or the accidental inspiration of vomited material may result in later pulmonary complications. If the patient should become even moderately conscious after the convulsion, as they frequently do, water can be freely administered by mouth or by the rectum after the bowel has been emptied by an enema.

Induction of Labor.—It is not advisable to make any efforts at delivery unless, for example, the head should be near enough to the outlet to permit of an easy forceps extraction, or unless, as in the case of a breech presentation, an extraction can be performed. The introduction of a bag in cases where the cervical dilatation has not progressed, or is not progressing satisfactorily,

may always be considered, although it should be limited to cases where the softening is well advanced and the bag can be inserted without previous instrumental dilatation. The modified Champetier de Ribes bag, or, as it is popularly known in this country, the Voorhees bag, is the best for the purpose. The digital method of dilating the cervix is tedious and time-consuming and lacerations are certain to result. The Bossi dilator and similar instruments are merely mentioned to be condemned.

Delivery.—With the rupture of the membranes, either spontaneously or artificially, labor comes on in many cases and may be allowed to proceed even while the other details of the treatment are being carried out. Hot packs seem to have a stimulating effect on labor pains and the baby, particularly if premature, is sometimes born in the blankets. Occasionally in a multipara with a soft, dilated, or dilatable cervix, and no engagement of the presenting part, version can be performed with advantage under ether anesthesia. In primiparae, however, in whom no evidences of labor are present, the attempt to induce labor when the cervix is not dilated is unjustifiable. It is better to continue the general sedative and eliminant treatment of these patients rather than resort to *accouchement forcé* with its necessary mutilations to the mother and possible death to the child. Conservation of the patient's strength is always of primary importance, and no procedure should be resorted to that would in any way reduce her chances of recovery.

Rectal Infusions.—If the patient is brought to a hospital (and this is always a great desideratum), more regular and efficient treatment can usually be instituted. After the initial enema and stomach washing, fluid should be given by rectum at regular intervals. This may be done by colonic irrigations or by simple rectal infusions of eight ounces of glucose solution (from 1 to 5 per cent), or soda bicarbonate solution (from 1/10 to 5 per cent). The main point in the irrigation is that it shall be sufficiently large in volume—from three to four gallons at a time, at a temperature of at least 110° F. At the conclusion of the irrigation a pint of the solution should be left in the rectum and the patient placed in a hot wet or dry pack if her physical condition indicates it. The presence of edema in a well-nourished patient should be taken as the deciding factor and I do not believe that small, emaciated women with low blood-pressure and little subcutaneous fat, or edema, should be subjected to the debili-

tating influence of a sweat pack. The irrigations alone are sufficient for them and natural perspiration may be awaited. The hot wet packs with an ice bag or cold towel applied to the head are not continued for more than twenty minutes and should be followed by a hot dry blanket in which the patient is kept wrapped for an hour.

The irrigations and packs may be repeated at intervals of from eight to twelve hours, according to the response, and if in the interim convulsions again come on, free recourse to morphin may be had. This drug after the initial doses and until a definite effect is secured, may be kept in reserve and further possible seizures

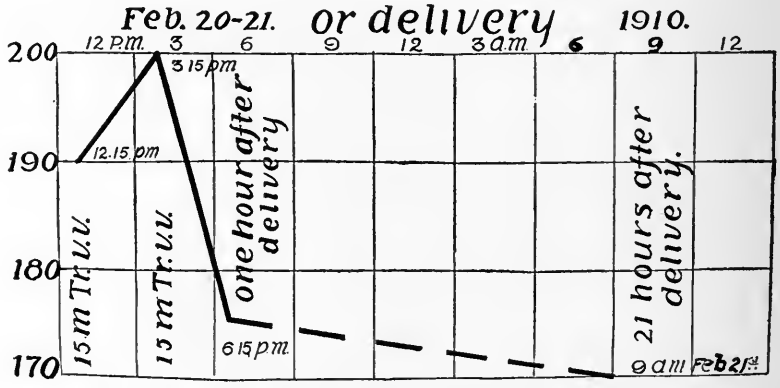

Fig. 26.—Blood-pressure Chart from a Pre-eclamptic, Showing Little Effect from Veratrum Viride (Bailey).

avoided by the administration of chloral hydrate and sodium bromid given in the first rectal infusion in doses of 40 grains of the chloral with one or two drachms of sodium bromid, or the official mixture of triple bromids. Blood-pressure observations during the first period often give a clue as to the effect of treatment by which a pressure of from 170 to over 200 before or after a seizure is sometimes reduced 20 to 30 points within a few hours. No effort should be made to reduce the blood-pressure beyond these figures, as it is necessary to keep up a full supply of blood in the organs of elimination and the skin. For this reason I do not advocate the use of veratrum viride, as it brings about a marked and rapid reduction often accompanied by severe depression and shock (Figs. 26–29).

Labor, Desirability of.—With the patient in the hospital a different view may be taken of the desirability of inducing labor.

If one is a convert to the extreme conservative therapy, no further attention need be paid to the induction of labor, for, as already stated, pains very often come on spontaneously. On the other hand, if one feels that the emptying of the uterus may lead to a more definite result, a suitable method of delivery may be selected which, however, should always be characterized by a minimum of shock and manipulation. This at once rules out *accouchement forcé* and the possible instrumental dilatation of the cervix advocated some years ago. Where the patient is near term, the presenting part engaged, the cervix soft, thinned out, and permitting the introduction of a bag, this can be inserted after the membranes are ruptured. On the other hand, given a primipara at the eighth or ninth month of her pregnancy with a rigid, undilated, thick cervix, a large baby, rigid soft parts and perhaps a slight degree of pelvic contraction, the abdominal cesarean section serves an excellent purpose, and if it can be properly done frequently saves the lives of both mother and child. Unfortunately the child often dies in cases where there have been many convulsive seizures, so even the disappointment of extracting a dead baby must not be regarded as a factor in the possible performance of the operation, because the mother is certainly subjected to much less mutilation and perhaps hemorrhage than in a forcible vaginal method of delivery.

Care of Patient after Labor.—Unfortunately, emptying of the uterus does not always bring about a cessation of the convulsions and they may be followed by a condition of deep coma lasting several hours and sometimes days. In no case should the eliminatory treatment of the patient be stopped after the uterus is emptied, and irrigations with or without packs should be continued at intervals of from eight to twelve or twenty-four hours until the patient's mind is entirely clear, the blood-pressure declines and the kidney function is good. The drinking of water during this period is essential, and if the patient can be roused the administration of diluted milk and cereal gruels is indicated. Chloral in 5-grain doses every four hours in capsule is a safe routine procedure after delivery and may be continued for several days until the declining blood-pressure gives evidence of satisfactory arterial dilatation.

Urine Examinations.—Urine examinations must be made at least once a day, care being taken to get clean specimens so that

the admixture of lochial discharges will not confuse the findings. A clean specimen may be secured by catheter; or, if the patient is conscious, by holding a sterile pus basin directly under the urinary meatus. The quantity of urine passed must be carefully noted, and if it remains much below 1,000 cubic centimeters in twenty-four hours, notwithstanding the irrigations and rectal injections, urination may be stimulated by a hypodermoclysis with normal soda bicarbonate solution (never with salt). In advanced cases marked by shock and extreme prostration there is no objection to the intravenous injection of the bicarbonate of soda or glucose solution (5 to 10 per cent). Not more than 600 or 700 cubic centimeters should be injected intravenously in order not to overstrain the mechanism of the heart.

After-care.—The after-care of eclampsia patients is important. As I have already stated they must be freely supplied with water and also with nourishment. The best form of nourishment is milk and cereal gruels supplemented by fruit juices a few days later. The breast secretion in eclamptics appears later than usual, and this is not unfavorable because nursing by the baby of an eclamptic mother must be absolutely interdicted for at least three days after delivery or until no further symptoms of the condition are present. Newborn babies who nurse eclamptic mothers have been known to develop eclamptic seizures as a result. If the breasts should become full before the three days have elapsed after delivery, they may be emptied by a breast pump and the milk thrown away. The condition of the urine in eclamptic patients improves rapidly, as a general rule, after delivery, but marked traces of albumin and an abundance of granular and hyaline casts may persist for many days. This means that the careful observation of the patient must be continued and rest in bed insisted upon until all evidences of renal irritation have subsided.

Complications, Treatment of.—The treatment of the complications associated with eclamptic convulsions must be treated as under other circumstances. Hemiplegia occurs occasionally, for which, of course, little more can be done than the treatment of the toxemia itself. The eye lesions, including blindness, must be referred to an ophthalmologist. Fortunately the visual disturbances are temporary in most instances, although retinal hemorrhages near the macula lutea may be productive of per-

manent damage. The traumatized tongue is often a source of considerable annoyance to the patient, particularly if associated with sordes. As the patient is unable to cleanse her teeth and mouth during the early days, oral hygiene must be carried out by the nurse, and the plentiful application of peroxide of hydrogen in half-strength applied with a cotton swab is very comforting and the use of some of the generally accepted mouth washes is also indicated.

Other Plans of Treatment.—Having outlined the general plan of treatment for toxemia in the later months of pregnancy which I have found most efficient and practical, I will consider in greater detail some of the many procedures advocated by others.

The two radically opposed camps so far as the treatment of the acute manifestations of eclampsia is concerned have, during recent years, gradually come to meet on a common ground and less is heard of absolute dependence on any one or other method of procedure. Stroganoff, of Petrograd, is probably the most widely known of the so-called conservative group, but even before his recommendations for treatment with mild doses of narcotics, Veit and Winckel both published their results of the treatment of the convulsions with larger, even massive, quantities of opium and chloral. Veit used frequently repeated doses of 0.03 gram, or a total of 0.2 gram, in from four to seven hours. In a series of 60 cases reported by him there were only 4 fatalities (6 per cent plus). Subsequently he advised in severe cases the use of warm baths and hot blankets. Veit did not approve of venesection.

Winckel was able at the same time to report a satisfactory method of controlling eclamptic convulsions with rectal instillations of chloral hydrate in doses of from 1 to 2 grams (15 to 30 grains), combined with chloroform inhalations. As much as 12 grams in twenty-four hours were given to some of these cases and the chloroform was administered until an effect was secured from the chloral hydrate. Winckel's series included 92 cases with a mortality of 7, or 7.6 per cent. No venesection was done in any of these cases. The results with this method were not invariably good and later on Winckel modified the plan by the addition of various operative procedures, evidently in cases that did not respond to the more conservative procedures.

The more reasonable employment of narcotics was suggested by Stroganoff. Although not at first entirely successful, further

experience with the method was followed by better results, and in the last series of 360 cases Stroganoff reports a mortality of 6.6 per cent. Unfortunately the details of the Stroganoff procedure are not strictly followed by many who claim to use the method, and the term is applied in any case where narcosis by morphin or chloral constitutes the essential factor in the treatment. Stroganoff calls particular attention to the necessity of placing the woman in a quiet, darkened room and avoiding all forms of irritation. Examinations, if necessary, should be made under light chloroform anesthesia. Another essential factor to which Stroganoff calls attention is the necessity for beginning treatment before the actual convulsions, whenever possible. In the procedure described by Stroganoff the initial hypodermic dose of morphin muriate is 0.015 gram, and one hour later 2 grams of chloral hydrate are given in solution in the rectum. Three hours later the morphin is repeated, and four hours after that the chloral. Thirteen and twenty-one hours after the beginning of treatment a dose of 1.5 grams of chloral hydrate is given by rectum. It will be observed that the interval between the administration of the drugs increases progressively. The employment of venesection is not recommended, but operative delivery may be resorted to in case the so-called prophylactic treatment is partly or wholly ineffectual. Such operations, however, Stroganoff limits to forceps and version under deep ether narcosis. Cesarean section and the introduction of the elastic bag, are not favored except in isolated instances.

Zweifel employed this procedure in his clinic at Leipzig in a large number of cases, as noted below, but combined it with venesection, abstracting not less than 500 cubic centimeters of blood as soon as the seizures began. In case the seizures did not seem to be affected in number or severity another venesection of 350 cubic centimeters was done. When a second venesection became necessary labor was always hastened. Zweifel also insists on thorough gastric lavage in obstinate cases, followed by the instillation of a quart of weak, plain lemonade or cream of tartar lemonade. Comparing his results with those obtained before the introduction of this method, Zweifel reports that when venesections with chloroform and morphin narcosis, hot packs, etc. (1887–1892), were employed, the mortality in 49 cases was 32.6 per cent. In a series of 623 cases treated by active

operative methods from 1895 to 1910 the total mortality was 17.4 per cent. Contrasting these results with the period during which venesection and the Stroganoff treatment was employed, the mortality in 94 cases fell to 5.3 per cent. The reduction in the fetal mortality is also noteworthy, having been reduced from 36 per cent in the operative period to 21.3 per cent during the time when conservative methods were employed. Zweifel discredits the statistics compiled by Liepmann and Freund, who report 8 deaths in a series of 18 cases at the Berlin Charité treated by the Stroganoff procedure. He considers this evidence insufficient and in comparison refers to their own mortality of approximately 15 per cent in the operative treatment.

Comparative Mortality Rates.—Winter also presents interesting comparative statistics based on the results of the treatment at his clinic, in which he used exclusively bloodletting and the Stroganoff method in order to make a comparison with his preceding methods of immediate delivery. While the conservative procedure is generally satisfactory, Winter believes that immediate delivery is superior in recent cases, especially delivery by vaginal cesarean section. On the other hand, when a long-standing intoxication is present, the results of immediate delivery are uncertain and the Stroganoff method should be preferred. In the cases in which the first convulsion was noted at the beginning of labor, the results were as follows: In 8 cases, in which labor was not interfered with, there was a mortality of 40 per cent; in 19 cases of delivery after the os was dilated, 30 per cent mortality; 32 cases delivered in the second stage by incision or bags, 25 per cent mortality; 34 cases delivered by early vaginal cesarean section there was 9 per cent mortality; in 22 cases by cesarean section immediately after the beginning of the attack, no mortality.

Lichtenstein also reports 80 cases treated by venesection and Stroganoff narcosis with 5 deaths, or 6.25 per cent mortality. In this series many spontaneous deliveries occurred and Lichtenstein calls particular attention to the reduction in the number of attacks, and to the fact that in 60 per cent of the cases no recurrence took place.

In this country increasing attention is now being given to the conservative methods of treating eclampsia, especially by narcotics. Among the most recent statistics is the report by MacPherson in an unpublished communication, including 104 cases

with 17 maternal deaths, or a mortality of 16.3 per cent. These patients were treated at the New York Lying-in Hospital and included many serious cases, 7 of which were actually moribund on admission. Omitting the latter, this would make a total mortality of only 9.6 per cent. The stillbirth mortality was 25.4 per cent. MacPherson compares these figures with the mortality of 30.8 in 250 cases reported by him in 1909 which were treated by purely operative measures.

A more radical conception of the treatment of eclampsia is that first advanced by Dührssen, who asserts that immediate operative delivery as soon as possible after the first seizure is always indicated. No previous narcosis was employed, for Dührssen declared that chloroform as well as morphin contributed to fatty degeneration of the heart muscle. As we now know, a simple degenerative process in the liver has also been shown to follow chloroform narcosis. In order to secure a rapid delivery Dührssen devised the operation known as vaginal cesarean section, although the procedure first originated by him included merely incision of the anterior and posterior lips of the cervix. Attention was immediately attracted to the value of this procedure by Dührssen, who reported that in over 93 per cent of his cases, convulsions ceased at once.

In this country we find Reuben Peterson has been the most active advocate of the Dührssen type of treatment. He made an extended study of 530 cases done by 118 operators. The collected statistics seem to show that the mortality was 23.4, which he compared with an average of 28.9 per cent after expectant treatment.

The fetal mortality likewise seemed to be lower, the sooner delivery took place after the first convulsion. The figures which Peterson presents of results obtained from conservative treatment certainly did not agree with those presented elsewhere and he went so far as to state that vaginal cesarean section is simple enough to be performed by any one with a fairly good knowledge of surgery and can be carried out in the home of the patient.

A similar study subsequently made by the same author is interesting in this connection. This later collection of statistics included 500 cases of abdominal cesarean section for eclampsia representing the work of 259 operators both here and abroad. In order to show the improvement in results Peterson grouped the cases chronologically. Between 1908 and 1913 there were 283

cases with 73 deaths or a maternal mortality of 25.79 per cent. Up to 1908 there were 198 cases with 95 deaths, or a mortality of 47.97 per cent. This shows a reduction in the maternal mortality of almost one half and is a reason, according to Peterson, why we should label as incorrect the older figures of a 50 per cent maternal mortality from abdominal cesarean section for eclampsia. He believes that the present mortality rate can be considerably lowered by care in technic and avoiding potentially infected cases. Although an eclamptic patient may die after a single convulsion, or may survive many convulsions, Peterson claims that the latter fact must be utilized as an indication of the degree of eclamptic poisoning until we have a better method of estimation. Emptying the uterus either spontaneously or by artificial means, while it puts a stop to the further elaboration of toxins from the fetus, the placenta, or both, may not be sufficient to prevent further convulsions, or in certain cases the death of the mother from intoxication.

In the 1914 Peterson series, convulsions ceased after abdominal cesarean section in 251 out of 457 cases, or in 54.92 per cent. This is in agreement with the general view that convulsions cease after the uterus is emptied in from 52 to 62 per cent of the cases. In 146 cases in which convulsions ceased after cesarean section there were 41 deaths, or 19.8 per cent mortality. This figure is said to be much lower than when the convulsions continue, since in 130 of such cases there were 41 deaths, or a maternal mortality of 31.53 per cent. Peterson insists that the operative treatment of eclampsia has not been given a fair trial, for the uterus should be emptied as soon as possible after the onset of the first convulsion and not after all kinds of medicinal treatment have been tried and failed. He finds an increase in mortality of 30.33 per cent due to delay, which is 10 per cent higher than after quick delivery. As regards the fetal mortality in Peterson's series, including all premature children and counting all children as living who survived one hour after delivery, there were 9 deaths in 248 cases, or 3.62 per cent. The fetal mortality, however, was 10.69 per cent if children dying the first three days after delivery be included. He believes, therefore, that better results are obtained for the fetus if the uterus is emptied early.

Peterson found that the maternal mortality is higher in cesarean section cases in multiparous women than in primiparous

eclamptics. In 225 primiparae the maternal mortality was 24.44 per cent, while in 48 multiparae it was 27.08 per cent. The fetal mortality was also increased, which he attributes to the greater degree of intoxication among multiparae. The maternal mortality also increases with the age of the patient. Peterson concludes that any obstetric condition which makes delivery by the natural passage prolonged and difficulty, may be accepted as an indication for abdominal cesarean section in eclampsia, although it cannot be denied that other methods of emptying the uterus give better results in eclamptics with normal pelves and soft parts and should not, therefore, be lightly discarded.

Cesarean Section, When Justifiable.—Whether abdominal cesarean section is justifiable in eclampsia has been questioned in a number of later contributions. Thus, Brodhead contends that in a large proportion of cases it should not be employed, although when the facilities are at hand it affords a satisfactory means of terminating the case. He collected 174 selected cases of cesarean section for eclampsia with a mortality of 28, or 16.1 per cent. This included one case each of sepsis, pneumonia, intestinal obstruction, ruptured uterus, and simple neglect. Subtracting these cases, the mortality was 12.2 per cent. There were 154 living children, of which 29 subsequently died, including premature and poorly nourished infants. In a later edition of 39 unpublished cases the mortality was 15.4 per cent, making a total of 213 sections with 34 deaths, or 16 per cent.

It is a difficult matter to form an absolute opinion as to the value of either vaginal or cesarean section in eclampsia. Undoubtedly the fetal mortality is lowered, especially if the operation can be performed soon after the first convulsion, but as these babies are often poorly nourished or develop toxic symptoms subsequently, the fetal death rate during the first few weeks should be taken into consideration. Moreover, operative deliveries of all kinds in eclampsia are productive of shock, and if shock be combined with excessive hemorrhage, the subsequent recovery of the patient is often doubtful. The operation with our modern methods is simple enough and has often been attempted by the tyro in obstetrics. My own belief is that it should be limited, as I have already stated, to primiparae at term with long rigid cervices that show no tendency to dilatation, combined with slightly contracted pelves and a rigid or perhaps narrowed outlet. With a

patient in good general condition who passes urine at least in moderate amounts, although not responding to the narcotic treatment after the first convulsion, it seems to me that the psychic factor enters into the question and that the doctor and family in many instances are overcome with a feeling of fear caused by the severity of the clinical picture, and lose to some degree, perhaps, their sense of calm and better judgment. Cesarean sections, either vaginal or abdominal, should not be undertaken except under the most satisfactory hospital surroundings, and the increasingly good results reported with more conservative methods should always be taken into consideration in deciding what shall be done in an individual case.

Venesection.—This is one of the oldest procedures in the treatment of eclampsia. As I noted in the historical introduction, medical writers for centuries have advocated opening an artery or a vein for the relief of convulsions, on the supposition that an overdistention of the blood-vessels was present, as manifested by the increased pulse tension, cyanosis and coma. In place of the actual opening of the vein, leeches applied to various parts of the head and body were formerly employed in some cases and believed to be particularly adapted to the more anemic type of women. The introduction of chloroform brought about a change in the views on this subject and venesection came to be regarded as harmful because the convulsions were ascribed to cerebral anemia. After this theory was shown to be groundless, venesection returned to favor, especially as the mortality in various clinics was found to increase during the period when no venesection was employed and before other methods of treatment were developed. As the rapid operative deliveries came into vogue the assertion was repeatedly made that it was not the operation of itself, nor the rapid emptying of the uterus that brought about a good result, but merely the loss of blood. The abstraction of from 300 to 500 cubic centimeters of blood from an arm vein in suitable cases is very generally employed, but according to the best teaching, it should be reserved for the cases of plethoric women in whom no improvement results after thorough narcotization has been secured. Thin, weak, anemic-looking patients should, under no circumstances, be subjected to venesection even when the blood-pressure is high. In post-partum attacks the abstraction of blood has been favorably regarded by many as a life-saving

measure, but its employment at this time should, it seems to me, be subjected to the same criteria as during the ante-partum period.

Technic of.—Venesection in eclampsia is preferably done in the median cephalic or basilic veins. The patient, if not in a narcotized state, should be given a few whiffs of ether and, after applying a tourniquet to the upper arm, a coating of tincture of iodin is painted on the flexor surface of the elbow, the vein is exposed by incising the skin over the same and a canula inserted and tied. A simpler procedure is to introduce a good-sized hypodermic needle or small trocar directly into the vein. The needle or canula is very apt to become obstructed at the beginning of the flow, by clots, and should then be withdrawn and cleaned with sterile water or salt solution.

Decapsulation of the Kidney.—The conception of eclampsia as a disease in certain cases of renal origin, led to a proposal by G. M. Edebohls to relieve the anuria by a decapsulation operation on the kidney. His first patient, a primipara, with severe repeated convulsions was delivered under chloroform by forceps after cervical incision. Post-partum convulsions and coma continued without response to the usual treatment in vogue and, "for the purpose of obtaining control of the uremia," decapsulation of both kidneys was performed three days after delivery. No further convulsions occurred and two days later all evidences of "uremia" disappeared with a complete restoration to health in a few weeks. Edebohls was so impressed by the result that he advocated the procedure before labor. A second case was operated upon a year later, also in a primipara, with marked edema, alternating delirium and coma, total blindness, almost complete anuria and beginning convulsions. Double renal decapsulation was performed, followed by great improvement in symptoms, and labor came on spontaneously forty-eight hours after operation with delivery of twins.

Case Reports of.—This somewhat radical procedure met with considerable attention after its publication. Sippel reported 42 cases with 12 deaths (28 per cent), a rather high mortality rate, but an anuria persisting for several hours, as in these cases, is usually fatal. In 3 cases reported by Zweifel, recovery took place and the urinary excretion underwent a satisfactory and constant increase soon after the operation. A more recent report is by Cardwell, who did a decapsulation and nephrotomy three days

after delivery in a patient with severe convulsions. Immediate improvement resulted.

The Edebohls' operation, while radical, may perhaps be of service in those severe cases in which anuria develops, but with the introduction of the other and newer methods of treating eclampsia the indications are not so frequently met with. If the decapsulation operation is decided upon in one of these serious cases, the kidneys are exposed, first one and then the other, through incisions along the outer margin of the erector spinae from the twelfth rib to the crest of the ilium, with the patient prone and the abdomen supported by an Edebohls' "kidney cushion." The fibers of the latissimus dorsi are then separated and the iliohypogastric nerve isolated and drawn to one side. The transversalis fascia is divided, the perirenal fat incised, and the kidney delivered if possible. The capsule is divided along the entire convex border of the kidney and stripped completely free with the gloved finger, after which it is cut away close to the pelvis. The kidney is dropped back into its fatty capsule and the wound closed, usually without drainage.

Skull Trephining and Lumbar Puncture. — Among other operative measures employed in eclampsia aside from delivery, mention may be made of the skull trephining procedure suggested by Zangemeister for the relief of intracranial pressure. In these cases a large osteoplastic flap was made, but the good results reported were not confirmed by others. It would appear that the same effect could be achieved by lumbar puncture and this has frequently been resorted to, from 5 to 10 cubic centimeters of cerebrospinal fluid being withdrawn. Among more recent reports, J. M. Snyder describes a case of severe eclamptic convulsions in a primipara twenty-five years of age in active labor, delivered by low forceps. Sedative and eliminant treatment was employed, but numerous severe convulsions continued with high temperature and rapid respiration. The patient was almost moribund when a lumbar puncture was done, and about two drachms of fluid allowed to escape. It was not under pressure and perfectly clear. Immediate improvement in the general appearance of the patient resulted, the cyanosis disappeared, the respirations became more regular and deeper and the edema slowly subsided. No further convulsions occurred and the patient made a steady

recovery, presenting a normal temperature on the third day with a return of consciousness.

Magnesium Sulphate, in Lumbar Puncture.—As an accessory to lumbar puncture, the injection of magnesium sulphate or of pregnancy serum has been recommended. Rissmann, who was probably the first to suggest the method, believed that the toxins of eclampsia involve primarily the cord and brain and, acting like tetanus, can be similarly affected by magnesium sulphate. In his first case, a primipara, the convulsions persisted after the birth of the child but ceased at once after the intradural injection of 5 cubic centimeters of a 15 per cent solution of magnesium sulphate in sterile water. In a contemporary article, Guggisberg denies the harmlessness of the procedure, and shows that the action of the drug in eclampsia is different from that in tetanus. Moreover, in order to obtain an effect, the magnesium sulphate must be injected at a higher level in the cord, which, while it may reduce the convulsions, is apt to have a dangerously paralyzing effect on the respiration. Both of Guggisberg's cases ended fatally, although in the second one, where the injection site was higher, the sedative effect on the convulsions was marked. Wallace advocated a 25 per cent sterilized solution of magnesium sulphate administered according to the weight of the patient, in the proportion of 1 cubic centimeter to every twenty-five pounds. He reported two cases, the first of which recovered after one injection and the second after two. Wallace also warns against the possible paralyzing effect on the respiratory center.

Normal Pregnancy Serum.—In place of the magnesium sulphate injection, Mayer suggested normal pregnancy serum as an antidote to the poison circulating in the central nervous system. This author reports two cases of advanced coma with pulmonary edema and history of convulsions. The prognosis was very bad but nevertheless the serum was given. In one case the patient apparently made a complete recovery, but in the other the disease was evidently too far advanced and the patient died soon after. In another instance, the baby of a mother who had had a mild eclampsia was seized with severe convulsions. Five cubic centimeters of spinal fluid was withdrawn and an equal amount of blood serum of a healthy pregnant woman injected. An immediate change for the better occurred and the convulsions ceased,

but the child died several hours later, apparently from cardiac weakness.

Rectal Infusions of Magnesium Sulphate.—To return for a moment to the antitetanic action of magnesium sulphate, we may refer to the rectal and subcutaneous methods of administration. Rissmann also suggested this method, combining the sulphate with veronal or luminal. He declared that morphin is contraindicated because of the danger to the fetal respiratory center, and chloral because it is a cellular poison. Six cases are reported in which luminal in doses of 0.04 gram injected subcutaneously either alone or, in the more severe cases, combined with rectal infusions of magnesium sulphate (from 10 to 15 grams to the liter), brought about a rapid subsidence of the convulsions and complete recovery.

Blood Transfusion.—On the theory that there is a substance in normal blood which neutralizes the toxins of the placenta, the transfusion of blood has been recommended in eclampsia. Blair Bell, almost a decade ago, reported a severe case in a primipara, in whom immediate improvement followed the intravenous injection of 500 cubic centimeters of the husband's blood. He claimed that transfusion is the best means of introducing antitoxins, which are also present in the blood of males.

Ductless Glandular Opotherapy and Serotherapy.—The belief that disturbances in the endocrine glands are etiological factors in the production of eclampsia has served as the basis for many therapeutic recommendations. It is essential to approach the problem with a great deal of caution. The thyroid is an example when decision as to whether one is dealing with hypo- or hyperthyroidism might better be left to an expert rather than determined by the obstetrician, unless the latter has been specially trained to recognize the symptoms associated with these more or less obscure conditions. Where a lack of thyroid secretion is evident, E. P. Davis advises small doses of the extract, one grain three times daily, continued for several months. Ward states that it is essential when Graves' disease is present, to determine whether it is a condition of hyperthyroidism or hypothyroidism. In the former, rest, icebags, milk diet, and sedatives should be employed, and if these measures fail, an antiserum, such as the cytotoxic serum of Rogers, may be administered. If hypothyroidism is present, thyroid substance should be given in the

form of the dry extract, or, if possible, a saline extract prepared from normal human glands. Ward believes that more reliance can be placed upon the nitrogen-partition of the urine as a guide to the severity of the toxemia than on the blood-pressure. Since this was written, however, the view as to the value of the nitrogen-partition test has undergone a marked change. Induction of labor is usually slow and uncertain in such cases, and, where there is a history of dystocia, elective cesarean section is preferable.

Although parathyroid extracts have been urged in the treatment of eclampsia because of the changes which these glands undergo in pregnancy, there is no warrant for this view because, as pointed out long ago by Seitz, the tetany produced by the removal of the parathyroids in pregnant animals is not necessarily the same as eclampsia.

Anomalies in placental function as a cause for eclampsia have been regarded as indications of hysterectomy (Zangemeister), and the "mammary theory" encouraged several German observers to propose complete ablation of the breasts for the relief of eclampsia (Sellheim, Herrenschneider, and Wagner), but these are extremist measures, no longer warranted in view of the good results which have attended less radical methods of treatment. The milking out of the colostrum from the breasts and also the intramammary injection of air or oxygen have been seriously proposed in treating eclampsia. These references are of interest, but much remains to be learned before such treatment can be satisfactorily employed.

Flushing through the Stomach.—The introduction of fluid into the circulation for the purpose of diluting the circulating toxins, throwing off the excess of salts and reducing the molecular concentration of the blood, is considered an essential of treatment, and in this connection we may refer to an interesting suggestion for flushing the system recently made by Davidson. In place of hot packs and irrigations, from two to three pints of water are administered through the stomach tube every four hours. In eleven cases this procedure was followed by profuse perspiration, and it can be done at home where efficient hot packs are often impossible. A far larger amount of fluid may be introduced than by the customary methods and satisfactory catharsis stimulated without resort to other measures. Regurgitation and aspiration

have not been noted but the water should be introduced quite rapidly and the tube removed at once. There is apparently no danger from acute gastric dilatation. The stomach was found to empty itself quite rapidly, no water being recovered when the tube was introduced four hours later. Davidson believes that in these cases we are dealing with a "toxic kidney block" rather than a true nephritis, and that the fluids introduced through the stomach are excreted by the kidneys more rapidly than if introduced into the rectum or intravenously, or into the tissues. He states that in cases where as little as two ounces of urine was secured by catheter at the beginning of treatment, thirty-two ounces were obtained eight hours later and a total of over one hundred and twenty ounces during the first twenty-four hours. With this treatment he also advises the administration of an ounce or an ounce and a half of Epsom salts and some alkali, such as twenty grains of potassium acetate or citrate, each time the tube is passed. Very possibly the latter have a pronounced diuretic effect. Davidson suggests that at least three lavages be done even after the patient is apparently out of the critical state.

Carbohydrates.—The employment of carbohydrates in the treatment of the toxemias of pregnancy has constituted one of the important developments of recent years in the management of this class of cases. The so-called carbohydrate deficiency theory is based on the assumption that the liver is the carbohydrate storing organ of the body and its cells filled with glycogen and that a carbohydrate deficiency in the maternal organism causes a glycogen depletion of the liver. Such a deficiency of carbohydrates during pregnancy may be of twofold origin: (1) there is an unexpected demand for glycogen on the part of the fetus, as shown by Slemons and others, and to a lesser degree by the rapid hypertrophy of the uterus; and (2) an actual deficiency, augmented in the presence of nausea and vomiting from lessened carbohydrate intake as the result of an improperly balanced diet. Titus and Givens, of Pittsburgh, have recently presented experimental evidence in an attempt to show that the liver function is impaired, especially in its detoxicating properties, and the body flooded with toxins after carbohydrate starvation. In other words, that a circulating poison is more toxic to an animal which has been fed low in carbohydrates. It was also found that the toxic effect of any poison is markedly diminished if given simul-

taneously with a dose of glucose. The favorable effects of excessive carbohydrate feeding in the vomiting of pregnancy has already been referred to in a previous paragraph, and in the more serious cases intravenous injections of carbohydrates in the form of glucose solution are known to give striking results. Titus reports in a more recent paper a series of 144 cases of vomiting of pregnancy, including 26 of the pernicious type, in which good results were thus secured and in only two was it necessary to perform an abortion. One of these was a fatal case and stated to be typical of acute yellow atrophy of the liver. The same authors have now extended this method to the toxemias of later pregnancy, and report a series of 20 cases in which intravenous injections of glucose were used in addition to a plan of treatment which may be denominated conservative, including the use of morphin, gastric lavage, purges, colonic irrigations and venesection, limiting interference with the pregnancy only when the patient's condition was improved or the fetus could be delivered without undue shock to the mother. In this series there were three deaths, a mortality of 15 per cent, whereas the rate previously with similar treatment but without the glucose injections had been about 29 per cent in the same hospital service.

In order to appreciate more fully the basis underlying the claims of Dr. Titus for the method, it is necessary to quote him somewhat more extensively:

"We maintain," he states, "that the pathologic progress of toxemia is dependent on a carbohydrate deficiency in the maternal organism, particularly in respect to the impairment of physiologic activity of the liver when unduly depleted of glycogen. It is indisputable, whatever the actual source of the toxins of pregnancy, that the liver and its functions plan an important part in the patient's ability or inability to recover. This is readily confirmed both clinically and pathologically, and, indeed, the distinctive pathology of certain necrotic lesions in the liver has been considered pathognomonic of various types of toxemia of pregnancy. Williams says, for instance, that peripheral necrosis of the liver lobules is the lesion to be found in fatal cases of eclampsia, whereas central necrosis is to be expected of acute yellow atrophy of the liver and pernicious vomiting of pregnancy. The entire distinctiveness of these lesions has been open to some ques-

tion in that there seems to be considerable diversity of opinion among such writers as De Lee, Hirst, Bumm, Berkeley and Bonney, and others regarding the pathology of eclampsia. Certain of our specimens from fatal cases of eclampsia have shown a predominance of peripheral degeneration, but central lobular changes also are clearly evident. The reverse is true of specimens

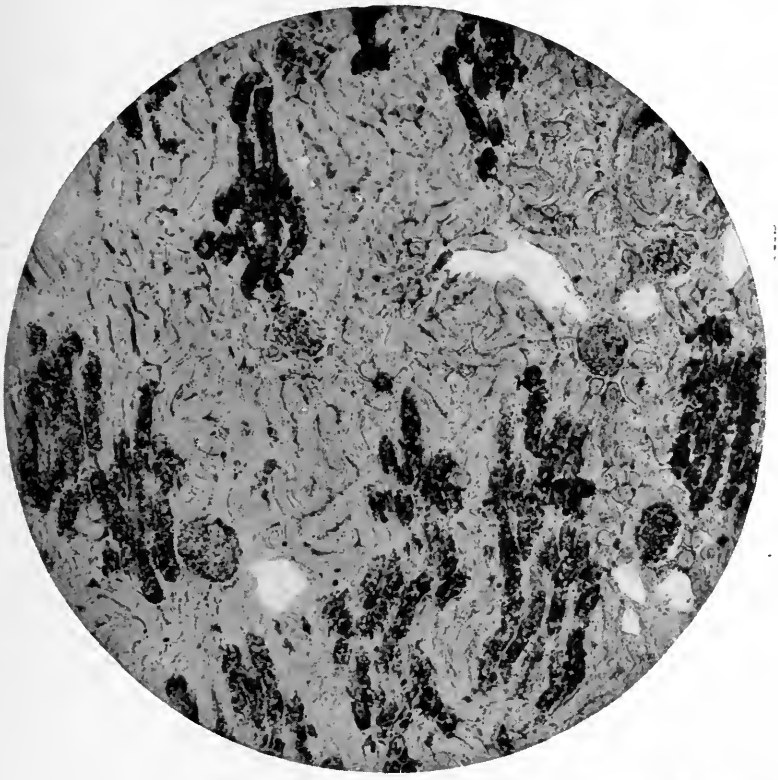

FIG. 27.—SECTION OF KIDNEY OF DOG (×50) SUBJECTED TO CHLOROFORM ANESTHESIA ON THREE SUCCESSIVE DAYS OR A TOTAL PERIOD OF FIFTEEN HOURS. Finally killed with chloroform on the fifth day. Stained to show the extensive fatty degeneration (Hull).

from cases of vomiting of pregnancy, in that the central necrosis is accompanied by a certain amount of peripheral degeneration of the lobules. This may be due entirely to relational differences between specimens; but, be that as it may, it is quite natural in any toxemia to expect both clinical and pathologic involvement of what is known to be the great detoxicating organ of the body. As a matter of fact, pathologic changes are evident in the liver

lobules after a lethal dose of almost every poison, whether it be organic or metallic.

"It is not intended to lose sight of the disturbances in kidney function which are almost invariable in eclampsia and, to a lesser degree, in other toxemias of pregnancy, but it is possible that they may be incidental to the action of these toxins as they are in pratically all cases of poisoning of any nature. For example,

FIG. 28.—SECTION OF KIDNEY OF DOG (×50) AFTER SEVEN AND ONE-HALF HOURS OF CHLOROFORM ANESTHESIA, SHOWING MARKED CONGESTION WITH CLOUDY SWELLING AND HEMORRHAGES INTO THE PARENCHYMA. Fatty degeneration is also pronounced (Hull).

nephritis occurs in the course of scarlet fever or pneumonia or after mercuric chlorid poisoning, as readily and as definitely as in hyperemesis gravidarum."

Intravenous Injection of Glucose.—Titus and Givens attempt to prove the claim that the damaged liver cells are restored to a marked degree by the intravenous injection of glucose by a series of

photomicrographs of sections of liver from certain fatal cases. These are compared with a section from an untreated case of eclampsia (see Figs. 27–30). It is claimed that the liver tissue from patients who received glucose intravenously shows far less pathologic change than is ordinarily to be demonstrated, the lobules presenting in many instances a fairly normal appearance. It is already well known that the regenerating powers of the normal liver are considerable.

FIG. 29.—SECTION OF LIVER OF DOG (×50) AFTER TWO HOURS OF CHLOROFORM ANESTHESIA. The liver appears yellow and fatty, with scattered hemorrhages. The cells about the centers of the lobules are entirely necrotic, a granular mass remaining. In some cases the liver cells almost entirely disappear with only a few scattered living cells in the portal spaces (Hull).

The technic of the preparation and injection of the glucose solution is very important, and, in addition, Titus believes that the determination of the blood-sugar at definite intervals makes it possible to plot a glycemia curve which is of prognostic value. It is essential that the glucose be of the highest purity. The fil-

tered solution must be sterilized under fifteen pounds pressure for thirty minutes. The amount of glucose injected varied from 15 to 75 grams dissolved in from 300 to 500 cubic centimeters of water—approximately a 15 per cent solution. The flow must be regulated so that the entire volume is introduced in about thirty minutes—the ordinary salvarsan apparatus with a clamped tube being sufficient for the purpose.

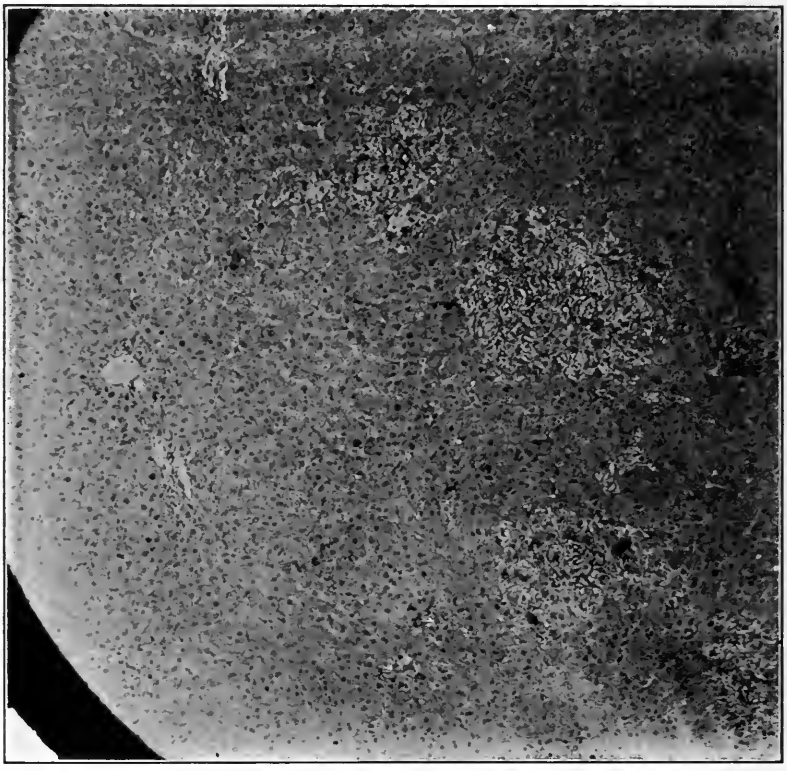

FIG. 30.—SECTION OF LIVER FROM A CASE OF TOXEMIA AFTER INTRAVENOUS GLUCOSE INJECTION. This section shows several "foamy" patches with normal tissue separating them. There is very little necrosis present and these areas are not well defined, being surrounded by numerous large cells with large, darkly staining nuclei, evidently a recent reparative process. This and the following illustrations (Figs. 31, 32, 33, personally contributed by Dr. Paul Titus) seem to show that typical necrosis associated with acute yellow atrophy and eclampsia is altered where intravenous injections of glucose have been employed.

Glycemia Curve as Index to Liver Impairment.—A further reference to the glycemia curve as an index of liver impairment may be made. Titus and Givens believe that the degree or extent of liver impairment in the presence of toxemia can be determined

by this means. Briefly outlined the steps are as follows and I am quoting them extensively for obvious reasons.

"A specimen of blood is taken for a blood-sugar determination, and a given amount of glucose is injected intravenously, taking a definite length of time for the injection, after which another specimen is taken for blood-sugar estimation. Blood-sugar read-

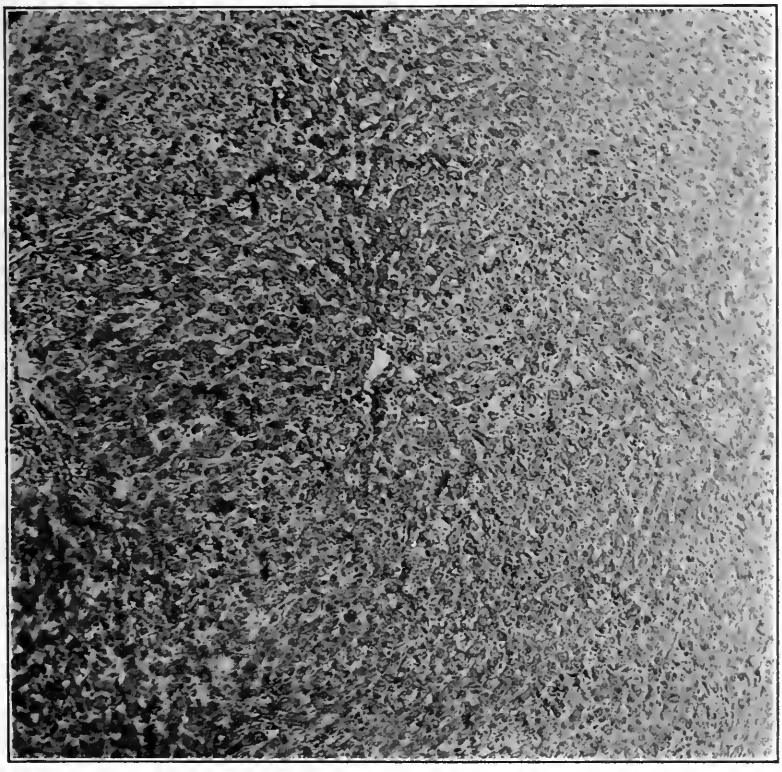

FIG. 31.—SECTION OF LIVER FROM A CASE OF ECLAMPSIA SHOWING SWOLLEN CELLS, POORLY OUTLINED, COARSELY PIGMENTED. Irregularity in size is noteworthy and the large amount of protoplasm suggests a process of repair (Titus).

ings follow at stated intervals and from them a glycemia curve may be plotted. It was thought that the rate of absorption and storage of the injected sugar would give an idea of the condition of the liver in the following respects: A liver depleted of glycogen but not infiltrated with fat should be greedy for sugar and take it up from the blood stream at a rate faster than under normal circumstances, whereas a liver which had undergone fatty

infiltration and necrosis would probably have its function in this respect impaired, even though it were more urgently in need of glycogen. It should be particularly pointed out that the glucose is injected primarily for its therapeutic effect rather than for the sake of this glycemia test, and that the taking of blood specimens involves no loss of valuable time in these serious and rapidly progressing pathologic conditions."

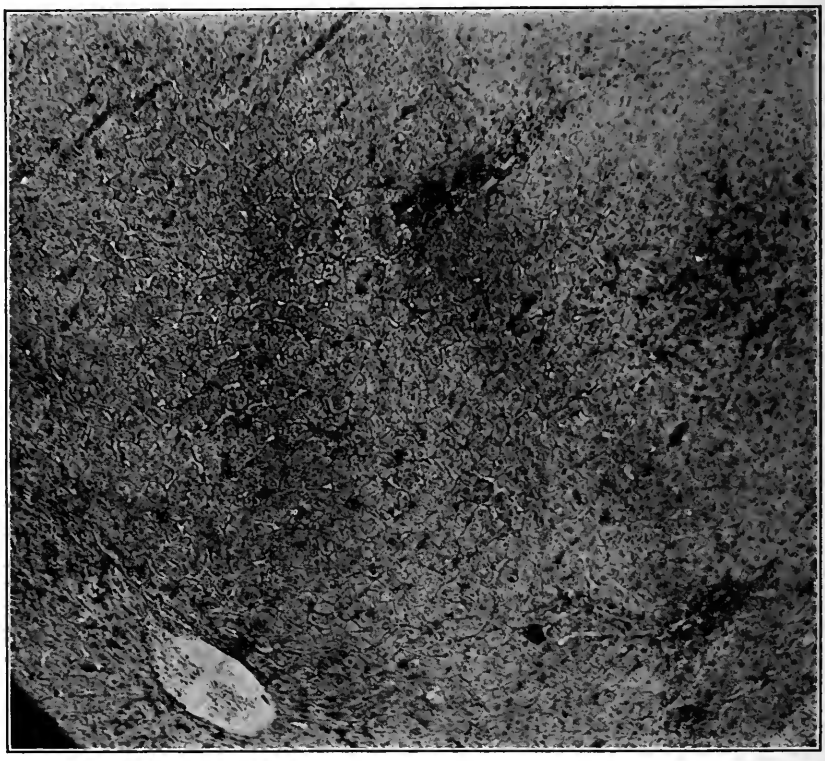

FIG. 32.—SECTION OF LIVER FROM A CASE OF ECLAMPSIA SHOWING EXTREME CLOUDY SWELLING OF CELLS, ALMOST "MOSAIC" IN APPEARANCE, OTHERWISE SIMILAR TO FIG. 31.

TECHNIC OF GLYCEMIA CURVE ESTIMATES

Five samples of blood are usually taken for sugar determination. The first, or control, sample is taken with the same needle through which the sugar is presently to be injected. Immediately after the blood has been obtained, the syringe is disconnected and the sugar solution tube attached to the needle. The time taken to complete the injection should be as near thirty minutes as pos-

sible. Five minutes after the injection is completed, Blood 2 is taken, then thirty minutes later Blood 3, and at one and two hours after Blood 3, Bloods 4 and 5 are obtained. Blood 1 serves as a control, Blood 2 represents the peak of the blood-sugar after injection, Blood 3 shows the reduction in blood-sugar thirty minutes after Blood 2, and Bloods 4 and 5 show whether or not the blood-sugar has returned to the level of Blood 1 during this allot-

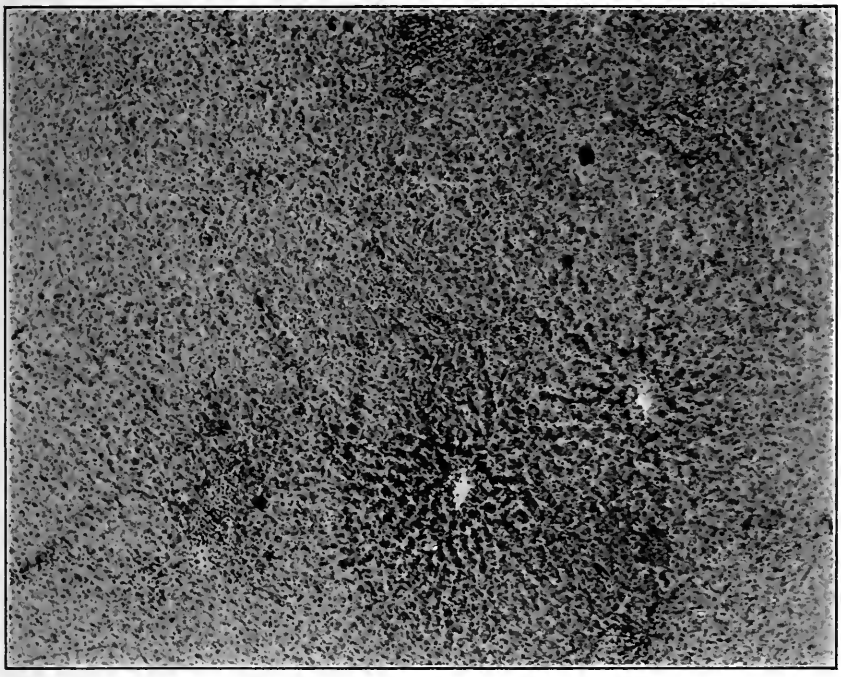

FIG. 33.—SECTION OF LIVER FROM A CASE OF ACUTE YELLOW ATROPHY IN EARLY PREGNANCY, SHOWING SWOLLEN, TURBID CELLS, OTHERWISE FAIRLY NORMAL. Slight increase of connective tissue in the periportal spaces and round-cell infiltration. Some cells contain fat globules, others coloring pigment. Many cells contain double nuclei indicating an active proliferating process. There is no evidence of necrosis (Titus).

ted interval. Bloods 2 and 3 are considered the most important, as they indicate the greatest amount of reduction in blood-sugar accomplished by the liver and tissues in thirty minutes.

Sugar in the blood should be determined by the Folin-Wu and the modified Folin-Wu procedures.

The results of a series of cases studied by Titus and Givens are given in the accompanying table.

Table of Cases Showing Glycemia Curve Estimations (*From Titus and Givens*)

Case	Hosp. No.	Age	Grav.	Bl. P. S—D	Urine		Glucose Injected Gm.	Blood Sugar (Mg. per 100 c.c.)					Difference Between Bl. 2 and 3	Comment	Result
					Alb.	Casts		Blood, 1	Blood, 2	Blood, 3	Blood, 4	Blood, 5			
Normal Controls															
1	K 2705	36	9	148–100	tr.	+	24.7	190	308	225	128	166	73	Trace albumin accounted for by fact urine voided, not catheter specimens in all normal controls	
2	P 2519	17	1	106–58	tr.	–	24.7	93	250	156	.....	.....	94		
3	C 2914	19	1	95– 70	tr.	–	25.0	113	241	135	94	76	106		
4	F 2825	18	1	110– 70	tr.	–	25.0	100	224	135	72	87	89		
5	G 3043	24	1	128– 84	+	+	25.0	83	208	140	89	83	68		
6	W 2686	21	3	110– 74	tr.	–	25.0	80	171	98	76	72	73		
7	L 3013	20	1	110– 78	tr.	–	25.0	89	185	113	81	88	72		
Chorea															
8	S 10738	..	2	....	+	+	23.0	66	238	157	117	....	81	Induction of labor	Recovered
	S 10738	..	..	....	+	–	20.0	90	185	132	101	116	53	Glucose injection repeated after recovery for control	
9	S 5870	20	1	138– 88	+	+	42.0	67	314	187	111	93	127	Induction of labor	Recovered
Toxemia with Premature Separation of Placenta															
10	B 4744	38	6	108– 60	+++	+++	15.0	181	283	212	141	150	71	Hysterectomy	Recovered
Hydatidiform Mole with Preeclamptic Toxemia															
11	R 7873	16	1	182–110	++	++	75.0	51	385	237	69	....	148	Marked toxemia	Recovered
Preeclamptic Toxemia															
12	C 3478	25	1	236–180	++	++	25.0	103	210	133	105	90	77	Induction of labor	Recovered
13	G 5504	28	7	170–124	++	++	25.0	143	348	235	140	111	113	Induction of labor	Recovered
14	D 5599	38	3	176– 90	++	++	25.0	71	160	100	63	62	60	Induction of labor	Recovered
15	M 8769	32	6	204–110	++	++	60.0	81	333	247	154	132	86	Induction of labor	Recovered

Pernicious Vomiting

16	H 3085 H 3085	.. ..	.. ..	128– 80	+ ..	+ ..	25.0 25.0	108 109	333 278	238 193	153 97	122 93	95 85	Jaundice, acidosis, etc. Glucose injection repeated after recovery for control	Recovered
17	O ——	..	1	....	..	..	30.0	100	345	235	118	132	110	Jaundice, acidosis, etc.	Recovered
18	D 5649	29	2	120– 90	+	+	30.0	125	351	250	165	147	101	Acute yellow atrophy of liver	Died
19	M 2235	..	2	98– 68	+	+	75.0	121	607	527	345	192	80	Emaciation, jaundice, etc.	Recovered

Eclampsia

20	H ——	31	1	204–150	+++	+++	25.0	143	266	230	182	174	36	Post-partum convulsions	Died
21	M 4287 M 4287 M 4287	.. .. ..	3	151–100	+++	+++	20.0 15.0 15.0	104 140 121	256 206 256	143 118 140	125 135 113	140 .. 109	113 88 116	Ten post-partum convulsions Second injection glucose for treatment Glucose repeated after recovery for control	Recovered
22	M 5081 M 5081	41 ..	9 ..	170– 90	+++ ..	+++ ..	15.0 15.0	114 85	182 219	133 127	121 106	129 100	49 92	Ante-partum convulsions Glucose injection repeated after recovery for control	Recovered
23	B 7010 B 7010	28 ..	.. ..	184–110	+++ ..	+++ ..	30.0 45.0	87 121	215 286	158 250	118 190	100 ..	92 36	Twelve ante-partum convulsions; repeated glucose slowly absorbed; multiple hemorrhages throughout body	Died
24	M 8695	..	4	172– 96	+++	+++	56.0	140	400	302	362	..	98	Four ante-partum convulsions	Recovered
25	A 3976	18	1	148– 98	+++	+++	30.0	105	238	157	85	..	81	Sixteen ante-partum and intra-partum convulsions	Recovered
26	J 961	..	..	172– 70	+++	+++	60.0	77	303	222	122	80	81	Eleven ante-partum convulsions, multiple hemorrhages in spleen, stomach, intestines, etc.	Died
27	B 9143	34	5	160–	+++	+++	75.0	84	488	345	..	..	143	Five ante-partum convulsions	Recovered
28	C 9345	18	1	140– 95	+++	+++	75.0	103	435	238	164	..	197	Six ante-partum convulsions with ablatio placentæ, hemorrhage and shock	Died

In Group 1 a number of full-term pregnant women, otherwise normal, are considered. The age limits are seventeen to thirty-six, the number of pregnancies one to nine. The blood-pressures are normal, and the urinary findings are hardly significant with the possible exception of Case 5. To each of these individuals 25 grams of glucose were given intravenously, and with the one exception of patient 1, who had had breakfast, all the blood-sugars before injection were within the normal range.

The second blood-sugars are interesting. The blood was taken five minutes after the injection was completed in order that sufficient time should have elapsed to insure a thorough mixing of the sugar with the blood. The lowest blood-sugar is 171 milligrams per hundred cubic centimeters of blood and the highest 308, yet all patients received the same amount of glucose. Thirty minutes later the corresponding figures were 225 and 98. Undoubtedly the size of the individual, the size and activity of the liver, and the activity of the muscular tissues account to some degree for the variations in the second blood. In the case of Blood 3 the reduction from the level of Blood 2 must be ascribed mainly to the liver because, of all the factors mentioned above, it is the variant of significance. In other words, the reduction of a blood-sugar from 0.308 to 0.225 per cent in thirty minutes is undoubtedly due to the activity of the liver cells in converting the sugar into glycogen and storing it as such. It has been suggested that our hypothesis regarding evidence for the storage capacity of the liver may not be entirely valid because of another factor which must be considered. If it may be assumed that there is no loss in injected sugar by way of the kidneys in these experiments, one must still think of the possibility that there may be a decrease in the capacity of the organism to utilize or destroy sugar, as well as a diminution in the ability of the liver to store glycogen. It is conceivable that the former circumstance might lead to a continued hyperglycemia; but it would seem that its influence on these readings would be slight, indeed, as compared to the broad limits of variation which we know to be possible in the liver. Loss of sugar by the kidneys is of little or no significance, especially in the presence of such complete breakage in kidney function as usually occurs in eclampsia.

The difference between blood-sugars 2 and 3 falls within certain limits for the group of normal individuals, the figures being

from 68 to 106, to be exact. If there is any marked disturbance of the glycogen forming and storage function of the liver, these figures should be altered thereby, and we have found such to be the case in eclampsia. It seems reasonable to assume, from data reported by others as well as from a study of the liver sections in the fatal cases, that this alteration is due to a pathologic condition of the liver.

Blood 2, or the height of the blood-sugar five minutes after the injection is completed, varies not only because of the factors hitherto mentioned, but also to a slight degree on account of the amount injected, if that be very large. If the same amount of sugar were given in each case, one might then be inclined to interpret a high blood-sugar for Blood 2 as indicative of liver disturbance, provided the tendency to remain high was still evident in Blood 3. At present we have no suggestion to offer regarding the level of Blood 2 because an inspection of the table shows several interesting facts difficult to explain. For example, the patients 2 and 6 of the normal group each received 25 grams of sugar, yet the blood-sugar 2 of the former was 250, and of the latter 171. The same peculiar variance will be seen in some of the pathologic cases.

Among the cases noted, the figure which seems to be an index of the activity of the liver which, in consequence, may be of prognostic significance is, according to the authors, the difference between the blood-sugars 2 and 3.

For the normally pregnant women as well as for the pathologic cases in which the patients recovered, the limits of these figures have been 49 and 127. Whenever the difference has been less than 50 we have considered the patient's condition grave, and 40 or less as practically hopeless. For example, patient 20, with a difference of 36 milligrams between the blood-sugars 2 and 3, died; case 23 was also fatal, the results of the first injection being suggestive of a grave condition. For therapeutic reasons this patient was given a second injection and, when a difference of only 36 milligrams was found, the case was considered hopeless. Patients 26 and 28 did not show a significant difference between the blood-sugars 2 and 3, nor did patient 18, who died with hyperemesis. The possible explanation of this is that they each showed temporary clinical improvement from the injection of glucose, a

fact confirmed later by the microscopic examination of sections of their livers. These sections indicate that there was considerable regeneration of the liver tissue, since the microscope does not disclose the characteristic lesions of pernicious vomiting in case 18, or of eclampsia in the other two.

It is evident from this important recent work that an immediate clinical improvement results in individual cases as well as a general lowering of the mortality rate. Chorea, preëclamptic toxemia and fulminating toxemias with separation of the placenta also showed favorable results. It is very probable, as demonstrated by the authors' observations, that the rate of absorption and storage of the injected sugar is an index of the condition of the liver, so that, if the process can be graphically noted, a prognosis based on such estimations is of value. The slower the rate of storage the more we may assume that there is an actual and extensive liver necrosis with loss of function and that as this improves an amelioration of the patient's symptoms and final favorable outcome of the case may be expected.

Summary

In attempting a final summary of the treatment of the toxemias of pregnancy, one is impressed by the fact that through the medium of better prophylaxis the incidence of these disorders of pregnancy is gradually diminishing and while a large number of cases is still met with, the prognosis, as a general rule, is greatly improved. A recognition of the underlying etiological factors in the individual case in so far as they can be determined, must continue to be the guide in the treatment. The laboratory and clinical findings should always be carefully weighed in their relation to each other, so that no undue importance is attached to any one feature of the case in determining whether the individual pregnancy can be allowed to continue in the presence of the disturbances of the early months or whether a change from conservative to radical treatment is demanded in the toxemia of the later months. The ingenuity of the medical attendant may often be taxed in dealing with a case of hyperemesis and the psychic element must be carefully considered, yet I firmly believe that con-

servative treatment is often carried too far and the emptying of the uterus is delayed too long in cases which are undoubtedly toxic and are irreparably damaged by the delay. On the other hand, the often sudden and alarming symptoms associated with the later toxemias develop a fear or even a panic in the attending physician that seems only satisfied by a radical procedure carried out at the expense of irreparable damage, and possibly of life itself.

Experience during recent years has shown that reasonable conservatism has met with good results and repeated collections of institutional statistics have demonstrated that the avoidance of shock in the handling of the cases has brought about remarkable reductions in morbidity and mortality. But there is still much to be done and no branch of obstetrics requires greater thought and attention on the part of those seriously minded to further improve the situation.

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CHAPTER V

URINARY CONDITIONS ASSOCIATED WITH THE TOXEMIAS OF PREGNANCY

By Frederic E. Sondern, M.D., New York

Ammonia coefficient — Amino-acids — Acidosis — Starvation — Bile pigment—Urine analysis with special reference to the diagnosis of toxemia of pregnancy—Volume — Solids — Urea — Chlorids — Indican—Albumin and casts—Nitrogen-partition — Acidosis — Urobilin and bile pigment — Differential diagnosis — Toxemias of pregnancy—Neurosis—Stasis and renal hyperemia—Nephritis.

The desirability of a periodic routine examination of urine in cases of pregnancy has long been an established custom and the need has been made even more apparent by the inclusion of various additional clinical symptoms under the designation of toxemia of pregnancy. While the chemical blood examination has added much to our diagnostic and prognostic knowledge in these cases, it has not replaced the more simple methods of urine analysis in the search for indications of toxemia as well as in the early differential diagnosis. Before considering in detail the significance of abnormal changes in the urine in pregnancy, a brief historical survey of the diagnostic procedures in toxemia may be of interest.

It has long been a popular belief that the urine of pregnant women suffering from hyperemesis, eclampsia and other abnormal symptoms is extraordinarily toxic to animals, but the more recent efforts to prove this theory by proper biologic tests tend to create some doubt in this respect. Thus, Zinsser's claim that he has demonstrated Pfeiffer's conclusion that a disintegration of albumoids causes anaphylaxis in hyperemesis and eclampsia, does not seem true in the light of more detailed investigation. The whole subject of the toxicity of the urine in pregnancy has been reviewed by Esch in connection with his research work and his conclusion is that relatively little of practical clinical value has been determined in this way.

The vigorous and persistent search to isolate a causative toxic substance was really not undertaken until the clinical entity of toxemia of pregnancy was established. The studies of James Young are a notable example, although the search for a toxin in the urine has remained fruitless to date and the research work which has been done, while in no sense conclusive, suggests that the urine is probably not the carrier of the toxin itself.

Soon after this correlation of the symptoms of toxemia of pregnancy as a clinical entity, the altered chemical composition of the urine in these cases was studied, but practically from the beginning the changes were considered a consequence of the toxemia, and in no sense the cause. The description of the urinary changes was much too technical for the average clinician of that day, and, being largely the result of the work of the biological chemist, the lack of proper emphasis that this altered body chemistry was the result and not the cause of the toxemia led to confusion in the minds of many. Every now and then articles still appear ascribing these anatomical changes in cases of toxemia of pregnancy to the abnormal conditions found in the urine; for example, to the acidosis, with complete disregard of the fact that at least equally severe faults of the same kind are found in the urine in cases of diabetes and in cyclic vomiting of children without the presence of the pathological lesions associated with toxemia of pregnancy.

Ammonia Coefficient.—The accurate differentiation of toxemia of pregnancy from cases in which similar symptoms were due to other conditions, notably nephritis, was formerly more difficult than it is to-day, and pathognomonic signs in the urine were eagerly looked for. It soon became apparent that an abnormal nitrogen-partition in the urine was the most pronounced feature, and particularly the increase in the relative amounts of ammonia and amino-acids. J. Whitridge Williams, in 1907, directed particular attention to the ammonia coefficient—the amount of ammonia nitrogen compared with the amount of total nitrogen in the urine. He not only believed that the relative increase in ammonia was in direct ratio to the severity of the toxemia, but that in this way it would be possible to estimate accurately the value of the treatment instituted to relieve the condition and also to decide how far a patient might be allowed to go before interference with pregnancy was justified. In the enthu-

siasm of having at last found a practical method to deal with a difficult decision, he established the rule that an increasing ammonia nitrogen of 10 per cent, or more, of the total nitrogen justifies interference with the pregnancy. Wider experience soon established a more conservative policy which Williams was among the first to adopt, but the fact remains that the ammonia coefficient is still one of the potent factors in determining just what Williams originally claimed—an index to the severity of the toxemia as well as an index to the point beyond which it is not safe to allow the pregnancy to go.

Amino-acids.—The advocates of the amino-acid determination or rest-nitrogen determination as guides to the severity of the toxemia soon lost ground, particularly on account of the more elaborate technical procedures involved, and eventually these methods were completely superseded by the ammonia coefficient determinations.

Acidosis.—The almost constant presence of acetone and aceto-acetic acid in the urine in cases of toxemia of pregnancy was believed to offer another means of judging of the severity of the condition. As the degree of acidosis evident in the urine in this way is, however, not necessarily a true index of the reduced alkalinity of the blood, the determination of the amount of acetone and aceto-acetic acid in the urine became less important and served as corroborative data only. The determination of acetone and aceto-acetic acid in the blood and of the carbon dioxid combining power of the blood plasma now offers accurate means of estimating the degree of the existing acidosis.

Starvation.—In cases of hyperemesis, or other symptoms of toxemia of pregnancy, there are often considerable periods during which the patient receives or absorbs little or no food, and the effect of this starvation on the ammonia coefficient as well as on the existing degree of acidosis is a most important factor, if these evidences are to be considered in estimating the severity of the toxemia. This does not mean that these aids in diagnosis are to be disregarded, or that their value becomes nominal for this reason, but it does mean that the possible effect of starvation must be taken into consideration when these determinations are used for diagnostic purposes.

Bile Pigment.—Owing to the serious import of the hepatic necrosis which occurs in toxemia of pregnancy, a careful watch

for bile pigment in the urine has been advised. Although delicate tests for bile pigment are used, the evidence of jaundice is usually apparent clinically before the pigment can be demonstrated in the urine. An excess of urobilin can, however, be found in the urine before bile pigment is demonstrated or evidences of jaundice are observed.

URINE ANALYSIS WITH SPECIAL REFERENCE TO THE DIAGNOSIS OF TOXEMIA OF PREGNANCY

Volume.—The daily amount of urine voided in pregnancy (from 900 cubic centimeters to 1,500 cubic centimeters) does not vary essentially from that in the nonpregnant state. The changes ordinarily noted in functional or organic renal disorders are the same; consequently, pronounced variations from the normal have the same significance. Neurotic polyuria is perhaps more common in pregnancy; and, when it occurs, justifies greater care in differential diagnosis than at other times. Frequency of micturition must not be interpreted as evidence of increase in volume.

Solids.—The normal limits in the amount of solids excreted in the urine are sufficiently wide to include what slight changes occur in normal pregnancy. Since the advent of blood chemistry, which determines accurately the presence or absence of nitrogen or other retention products, the amount of urinary solids is relatively of no importance except perhaps to indicate the desirability of a chemical blood examination.

Urea.—The normal minimal daily excretion of urea in pregnancy is about 16 grams, but there is usually a somewhat reduced excretion immediately after parturition. Now and again cases are met with in which this reduced excretion is abnormally pronounced and is as low as 10, 8, 6, or even 4 grams, without other abnormal signs in the urine or any adverse clinical symptoms. This occurrence has always been the cause of anxiety and can now be avoided by determining the absence of nitrogen retention in the blood.

Chlorids.—The significance of chlorid retention in pregnancy has been emphasized chiefly by the German writers, but the determination of the amount of chlorids excreted in the urine is not used generally as a diagnostic aid, as it is replaced in a way

by definite clinical signs in the differential diagnosis concerned. Normally about 10 grams are excreted in twenty-four hours, which amount is subject to considerable fluctuation caused by the diet. In a consideration of the subject of urine analysis in pregnancy it would be impossible to discuss the significance of chlorid briefly, but the question is an involved one and has, or is usually considered to have, little, if any, relationship to the toxemia of pregnancy. Zinsser, however, attaches the greatest importance to chlorid retention in eclampsia and obtains most important diagnostic and prognostic information from his chlorid estimations.

Indican.—An excess of indican in the urine is usually referred to abnormal fermentation or putrefaction changes in the intestinal tract. Such an occurrence is undesirable in pregnancy and the indications for correction of these alterations are obvious. Accurate quantitative determinations are laborious and unnecessary, the usual tests being quite sufficient to determine the presence of an excess which has clinical significance. It is a well-established observation that toxemia of pregnancy is very often associated with an indicanuria, and in a large number of cases the records indicate that a constant excess of indican had been present in the urine of these patients even before pregnancy. Without the effort or the ability to prove an association between intestinal toxemia and the toxemia of pregnancy, practical experience has demonstrated at least coincident occurrences of this condition in many cases. For this reason careful attention to the elimination of intestinal toxemia is advised as a prophylactic measure.

Albumin and Casts.—The frequency of albuminuria in pregnancy has long been recognized, and it is generally understood that about 50 per cent of pregnant women show albumin in the urine at some time during the period of gestation. This, of course, includes slight traces of albumin which are demonstrated on careful analysis of filtered specimens. It is also an established fact that the relative amounts of albumin in the daily amount are not guides either to the nature or the severity of the existing cause. The presence of albumin without the presence of casts, or of larger amounts of albumin with very few hyaline casts, are more apt to be due to a functional disorder of the kidney in pregnancy than in the non-pregnant state, while a true nephritis of one or other of the types will present the usual composite picture

of the respective lesion. The amount of albumin found may vary from a slight trace to 10 or more grams per liter by weight. Whenever the presence of albumin is demonstrated it becomes an imperative duty to determine the cause so far as this is possible in order that proper measures be instituted. Many women are made miserable, and many babies are handicapped, by the assumption that any albuminuria indicates the presence of a nephritis.

There is nothing characteristic about the albuminuria in toxemia of pregnancy. Ordinarily traces of small amounts of albumin are present without casts or with perhaps an occasional hyaline cast coincident with the slight or the more severe symptoms of toxemia. Only a short time before, or at the time of, an eclamptic seizure, the urine may suddenly present every characteristic of a severe acute nephritis with one notable exception, namely, the signs often completely disappear from the urine in an incredibly short period after the cessation of the eclamptic attack, an observation never made in acute nephritis due to any other cause.

Nitrogen-partition.—The important features in the faults found in the nitrogen-partition of the urine in cases of toxemia of pregnancy are the decrease in the relative amount of urea nitrogen with an increase in the relative amount of ammonia nitrogen, amino-acid nitrogen and rest nitrogen. From a practical clinical standpoint it is essential to reduce the technical procedure to a minimum in order to make the method as simple and as rapid as possible, so long as it renders all the information which the method is capable of furnishing. This is accomplished by the estimation of total nitrogen, urea nitrogen and ammonia nitrogen, and calculating the percentage of the total nitrogen the two latter figures represents. This determination can be made by any of the approved methods. The urea nitrogen cannot be estimated by the hypobromite method, as it is not sufficiently accurate at any time, and is particularly faulty when there is an increase of ammonia nitrogen. In normal urine the amount of total nitrogen is about 8 grams in twenty-four hours; the urea nitrogen about 6.5 grams, or 85 per cent of the total nitrogen; and the ammonia nitrogen about 0.3 gram, or 3.5 per cent of the total nitrogen. In cases of toxemia of pregnancy, as stated before there is a decrease in the urea nitrogen from 85 per cent of the total nitro-

gen to 70, 60, 50 per cent, or even less; and an increase in the ammonia nitrogen from 3.5 per cent of the total nitrogen to 5, 10, 20, 50 per cent, or more. In estimating the significance of this relative increase in the amount of ammonia nitrogen in cases of toxemia of pregnancy, a gradually ascending increase with increasing evidences of an acidosis, although the patient has been under suitable treatment, is much more unfavorable than a single very high percentage which can often be reduced to the normal by an enema containing a sufficient amount of glucose. The probable influence of starvation must not be forgotten at any time, and the effect of the increasing retention of food should be reflected in a corresponding decrease in the ammonia nitrogen percentage if this is an important factor.

Acidosis.—Smaller or larger quantities of acetone and of aceto-acetic acid are usually present in the urine in cases of toxemia of pregnancy. Were these quantities only approximately indicative of the amounts in the blood, a quantitative estimate would serve a very useful purpose, but as this is not the case, the usual tests which indicate their absence, or presence, in small, moderate, or large amount are quite sufficient. These simple observations in addition to the other tests made, serve a useful purpose in estimating the severity of the toxemia, and offer a good indication for the need of determining the carbon dioxid combining power of the plasma, and the quantitative estimation of the acetone bodies in the blood. Starvation has, if anything, a greater effect on acidosis than on the ammonia coefficient, and this must be borne constantly in mind when interpreting the results of these examinations. Lactose is found in the urine in pregnancy in a relatively large number of cases, and it is sometimes not differentiated from glucose, but as there may be a coincident acidosis of toxemia, the possibility of a wrong diagnosis of diabetes due to faulty observation is apparent.

Urobilin and Bile Pigment.—The occurrence of jaundice in toxemia of pregnancy is one of the later and more serious signs, and the appearance of bile pigment in the urine is a symptom watched for with anxiety in these cases. The urine, generally small in amount and concentrated in character, is usually highly colored and the positive demonstration of bile pigment is not a simple procedure. In fact, the clinician is usually able satisfactorily to demonstrate evidences of jaundice before bile pigment

is positively identified in the urine. The relatively early recognition of an excess of urobilin is a common experience, but it is often difficult to decide whether the apparent excess is due to mere concentration or is actually a sign of hepatic, functional or other disorders. At all events, the significance of an excess of urobilin and the presence of bile pigment should be kept in mind; and, finally, it must not be forgotten that simple jaundice due to duodenal catarrh can also occur in pregnancy with no relation whatever to a true toxemia.

DIFFERENTIAL DIAGNOSIS

Toxemia of Pregnancy.—In hyperemesis associated with pregnancy there is a decrease in the daily amount of urine (400 cubic centimeters to 800 cubic centimeters being common figures); an increase in specific gravity with other evidences of concentration; generally a tract of albumin without the presence of casts; and a decrease in the daily amount of urea due to the restricted intake of food, and the changes in the nitrogen-partition. If the ammonia coefficient and the presence of evidences of an acidosis in the urine have been determined from time to time, gradually increasing amounts of acetone and aceto-acetic acid will be noted. If, however, a single estimation of the ammonia coefficient is made at this time, it is possible that an alarming figure may be obtained. The institution of efficient treatment incidentally will result in a decided improvement in these diagnostic signs of toxemia.

Under these circumstances the continuance at regular intervals of the observations described above is all that is necessary to confirm the clinical signs. The frequency of the examinations naturally will be guided by the clinical symptoms, on the one hand, and the laboratory findings, on the other. While a slight or moderate toxemia continues, the ammonia coefficient will probably fluctuate between 5 per cent and 8 per cent with occasional evidences of a mild acidosis due wholly, or in part, to the restricted food intake. If at any time the symptoms are out of proportion to the laboratory findings, additional determinations are urgently advised. Severe headaches, ocular signs or cardiac disturbances with, or without, abnormally low total nitrogen or urea excretion should prompt a chemical blood examination to

exclude a nitrogen retention. Clinical symptoms with the least indication of acidosis should indicate determination of the carbon dioxid combining power of the plasma determination and the estimation of the acetone bodies if necessary. On the other hand, if the urine examinations show evidences of increasing disturbances, even though the clinical condition is relatively satisfactory, and particularly if the ammonia coefficient continues to increase, a sharp lookout should be kept for an excess of urobilin, bile pigment and evidences of nephritis. The study of a considerable number of these cases demonstrates that the decision as to how long a pregnancy should be allowed to continue under these circumstances does not depend on any one determination, or even on any group of determinations. The fact remains, however, that these aids are essential in reaching a conclusion, although perhaps more so in one case and much less so in another.

The condition just described may result in eclampsia. The development may or may not be preceded, but is invariably accompanied, by all the evidences of an acute nephritis in the urine. There is usually a longer or shorter period of complete anuria, followed by a very scanty excretion of highly colored urine containing a large amount of albumin and a considerable admixture of blood. Usually there are also vast numbers of all kinds of casts, chiefly epithelial and granular, although for a short period at the very beginning no casts at all may be found. This urine picture continues during the eclamptic period. If the convulsions and the toxemia end in the emptying of the uterus, which is often, but not always, the case, it is almost incredible how rapidly the abnormal features may disappear from the urine. It is not an unusual experience to receive a perfectly normal specimen of urine from a case of this kind six hours after the uterus has been emptied, thus terminating a most violent attack. It is in this respect that these cases differ so noticeably from the cases of uremia in pregnancy with convulsions in which the kidney recovers, if at all, in the usual slow manner noted in a similar condition in the nonpregnant. If the urine is examined for the first time during the convulsive attack it presents no evidences which will aid in the differential diagnosis between a toxic eclampsia and nephritic uremic convulsions in pregnancy.

Neurosis.—In women of neurotic temperament a condition simulating true hyperemesis is sometimes observed. In most

instances the loss of food is more imaginary than real, and the urine shows none of the evidences of toxemia or even the slightest sign of acidosis due to starvation. If, however, the vomiting does interfere with nutrition, acetone bodies may appear in the urine and there may be a moderate increase in the ammonia coefficient, but the figures are never alarming and usually promptly return to the normal after efficient treatment. A paroxysmal neurotic polyuria is not uncommon in these cases and the decreased excretion of solids is usually relative only. Even if associated with a temporary acidosis the picture scarcely ever simulates a true toxemia and a subsequent examination makes differentiation a simple matter.

Stasis and Renal Hyperemia.—Occasionally cases are met with in which stasis due to pressure and consequent renal hyperemia gives rise to albuminuria varying in severity and with no constant accompanying evidences in the urine. The amount of urine may be large or small, and the albumin varies from a slight trace to a considerable amount, usually without the presence of casts. The daily amount of solids is normal and there are no evidences of toxemia, unless by chance this is an associated condition, no instance of which is recalled. The positive differential diagnosis is difficult for the very reason that positive evidences are lacking, and it must, therefore, rest on the absence of both the clinical and the laboratory evidences of an actual renal lesion.

Nephritis.—Pregnancy, without doubt, occasions a considerable additional strain on renal function and the presence of an organic lesion of the kidney thus becomes an important question in safeguarding the pregnant woman. The subject of nephritis in pregnancy remains an involved one, and is further complicated by a certain relationship between toxemia of pregnancy and faulty renal function, if not an actual renal lesion. For the purpose of simplifying the diagnosis there is a constant effort to separate toxemia of pregnancy from disordered renal function and actual kidney involvement, or at most to consider the former a cause of the latter, but the fact remains that convincing proof of actual disassociation is still lacking.

Acute.—Acute nephritis, as an intercurrent complication in pregnancy, due to any one of the usual causes, runs a course much the same as in the non-pregnant state, except that, everything else being equal, the prognosis is not quite so favorable. The urine

picture may be exactly that noted in toxic eclampsia or in acute exacerbation of a chronic nephritis, and, while differentiation at the moment may be impossible, comparison with the previous records will at once permit the proper classification. The subsequent course of the disease is also characteristically different in all respects.

Chronic Interstitial.—Chronic interstitial nephritis is unquestionably rare in women during the child-bearing period. It does occur, however, and, when present, may show no clinical symptoms and such slight signs in the urine that its existence may be completely overlooked. The fact that a nephritis of this type, of such severity as not to allow the completion of pregnancy, and may be present with but a faint trace of albumin and a few hyaline casts in the urine, is the very reason why these evidences found at any time should justify a painstaking clinical and laboratory investigation to determine their cause. It is in these cases particularly, or in cases in which this condition is suspected, that the determination of the presence or the absence of nitrogen retention in the blood has its greatest merit. These are the cases in which sudden acute uremic convulsions which so closely resemble a toxic eclampsia, may occur, that the urine examination records and the slower recovery in uremia patients, if they survive, offer the only means of differentiation.

Chronic Parenchymatous.—This form of nephritis, more or less quiescent, is the type of Bright's disease most frequently encountered in pregnancy. While it is possible for a nephritis to develop during pregnancy, it is much more probable that the lesion was contracted during an infectious disease in childhood and remained quiescent until greater functional demands were made on the kidney in the pregnancy. This type of nephritis is never overlooked in a properly made urine analysis, as easily demonstrated amounts of albumin, pus cells and casts are always found even in the quiescent stage of a but slightly developed lesion. While a parenchymatous nephritis may allow the completion of a pregnancy, its presence is always the cause of much anxiety and demands most careful management even in the mild cases. As there is no pronounced nitrogen retention in this type, blood chemistry does not offer the helpful diagnostic and prognostic information thus obtained in cases of interstitial nephritis. Uremic convulsions may, however, occur most unexpectedly, and

then the urine suddenly assumes all the characteristics of an acute nephritis. Now and again a chronic parenchymatous nephritis is associated with a true toxemia of pregnancy, and this combination may offer a most difficult diagnostic and prognostic problem—one which will tax the ingenuity of the most astute clinician.

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CHAPTER VI

SIGNIFICANT CHEMICAL CHANGES IN THE BLOOD IN THE TOXEMIAS OF PREGNANCY

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Chemical analysis—Nonprotein nitrogen—Urea nitrogen—Rest-nitrogen—Uric acid—Creatinin—Chlorids—Alkali reserve—Carbon dioxid, how determined—Blood changes in—Nephritic toxemias—Blood changes—Acute yellow atrophy of the liver—Blood changes—Hyperemesis—Blood changes—Carbon dioxid combining power, decrease of—Pre-eclampsias and eclampsias—Blood changes—High nonprotein nitrogen—Urea and rest-nitrogen—Uric acid concentration—Creatinin and chlorids—Hyperglycemia—Nonprotein nitrogen distribution—Umbilical vein and artery—Cerebrospinal fluid—Summary.

Chemical Analysis.—The introduction of accurate and rapid methods for the chemical analysis of blood, largely through the work of Folin, Benedict, Van Slyke and Myers, has given a new impetus to biochemical investigation within the past ten years. The application of these methods to the study of chemical changes in the blood in various pathological conditions has yielded information of immense practical value in the diagnosis, prognosis and treatment of metabolic and constitutional diseases. Although in this chapter our object is to emphasize only those points in the chemical analysis of the blood which may serve as a guide in the diagnosis and treatment of the toxemias of pregnancy, it is essential at the outset to discuss briefly the composition of normal blood and the variations associated with the more common metabolic disorders. For practical purposes an analysis of the blood should include a determination of the nonprotein and urea nitrogen, uric acid, creatinin, the total chlorids (as NaCl), sugar, and the carbon dioxid combining power. In some instances a knowledge of the diastatic activity and the cholesterol content of the blood is of great value. For a description of the technic employed in these analyses it will suffice to refer to the work of Myers.

Nonprotein Nitrogen in.—The nonprotein nitrogen constitutes about 1 per cent of the total nitrogen of the blood: variations in the protein nitrogen have no direct bearing upon the conditions which we are considering in this discussion. It will be evident from Table I that 100 cubic centimeters of normal blood contain from 25 to 30 milligrams of nonprotein N, and from 12 to 15 milligrams of urea nitrogen. The nitrogen in the urea molecule is the chief component of the nonprotein nitrogen. Mosenthal and Hiller have pointed out that a selective action of the normal kidney maintains the urea nitrogen at a level of 50 per cent, or slightly less, of the total nonprotein nitrogen, but, an impairment of kidney function, even of a slight degree, may result in an increase in the percentage of the urea nitrogen. In advanced cases of renal involvement, as Myers has shown, there is a marked increase in the nonprotein and the urea nitrogen, but the urea nitrogen constitutes from 75 to 85 per cent of the nonprotein nitrogen. The urea is largely synthetized from the ammonia produced in the deaminization of the amino-acids resulting from the protein digestion. It is, then, almost entirely of exogenous origin. Obviously the character of the diet will influence to some extent the nonprotein and urea nitrogen content of the blood. The nitrogen of the food is transported by the blood to the various parts of the organism for the repair of old, or the building of new, tissues. The waste nitrogen is carried directly or indirectly to the kidneys for elimination by the same medium. Hence, after a meal containing protein, there may be a temporary elevation of the nonprotein and urea nitrogen of the blood. Tileston and Comfort have reported in healthy subjects a rise in the nonprotein nitrogen of from 2.9 to 8.5 milligrams and in the urea nitrogen of about 2.5 milligrams, two and a half hours after consuming a heavy meal. The relation of the urea to the nonprotein nitrogen, however, was not disturbed by the intake of food. It is essential, therefore, for a comparison of results, that specimens of blood should be drawn under conditions as nearly uniform as possible. The best procedure is to obtain the blood in the morning before breakfast, that is, after a fast of from 12 to 14 hours. This will eliminate any changes in composition due to the recent ingestion of food.

Retention of.—The conditions in which a retention of nonprotein and urea nitrogen may occur are very numerous. A marked

TABLE I.—Significant Chemical Changes in the Blood in Disease

Condition	Urea, N	Sugar	CO_2-combining Power	Creatinin	Uric Acid	Nonprotein-N	Cholesterol	Chlorids as NaCl	Diastatic Activity
	mg. to 100	Per cent	c.c. to 100	mg. to 100	mg. to 100	mg. to 100	Per cent	Per cent	
1. Normal	12–15	0.09–012	50–75	1–2	2–3	25–30	0.14–0.17	0.45–0.50	15–20
2. Beginning pathologic	20	0.15	–45	3.5	4	35	0.19	+0.52	25
3. Renal diabetes		0.08–0.12							
4. Mild diabetes		0.15–0.30							25–40
5. Severe diabetes	20	0.30–1.20	50–10	2–4	4–10		0.2–0.8	0.40	35–75
6. Gout					4–10				
7. Early interstitial nephritis	15–25	0.12–0.15		2–3.5	5–12			0.45–0.60	
8. Acute nephritis	40–100	0.12–0.18	45–20	2–6	5–15			0.45–0.60	
9. Parenchymatous nephritis (nephrosis)	20–50	0.12–0.20		2–4	2–5		high	0.50–0.61	
10. Terminal interstitial nephritis	60–300	0.12–0.24	40–12	5–28	5–27	100–350	to 0.30	0.36–0.60	20–50
11. Bichlorid poisoning, to	300	0.12–0.20		33	15	370	0.35		
12. Double polycystic kidney, to	75	0.20		8	5				
13. Prostatic obstruction	12–40	0.11–0.16		1.5–3.5	3–9				
14. Acute intestinal obstruction	45–120					75–170			
15. Eclampsia	6–25	0.09–0.14	58–10		3.6–11.0	29–90			
16. Cholelithiasis							0.13–0.30		
17. Pernicious anemia							to 0.09		

accumulation of these products is found not only in the advanced stages of nephritis of the interstitial type, but also in such conditions as bichlorid poisoning, double polycystic kidney, malignancy, pneumonia, cardiac conditions, syphilis, and gastric and duodenal ulcer. In all of these diseases, however, the retention is due to renal complications, but as in nephritis when the urea nitrogen is retained, it forms more than 50 per cent of the nonprotein nitrogen.

Urea Nitrogen in.—Since the urea nitrogen is the chief component of the nonprotein nitrogen, and its estimation is considerably simpler, the determination of the urea nitrogen is generally adopted in clinical work as a diagnostic index of kidney function. A knowledge of the concentration of the nonprotein nitrogen of the blood alone is of no definite value, but the relation of the urea nitrogen to the nonprotein nitrogen is of prime importance in the toxemias of pregnancy.

Rest-nitrogen in.—A subtraction of the nitrogen contained in the well-known nitrogenous waste products from the total nonprotein nitrogen of the blood gives a fraction called the rest-nitrogen, which comprises the nitrogen contained in a series of little-known compounds. Among these the amino-acids are probably the most important. The amino-acid nitrogen of normal blood ranges from 4 to 6 milligrams per 100 cubic centimeters, but for a short period following the intake of proteins in the diet, it may rise to from 6 to 8 milligrams per 100 cubic centimeters.

Distribution of Nonprotein Nitrogen.—A comparison in Table II of the relative distribution of the nonprotein nitrogen of the blood among its known components emphasizes several points of interest. It will be noted that in health the urea nitrogen forms about 50 per cent of the nonprotein nitrogen, and the rest-nitrogen about 46 per cent. In parenchymatous nephritis there is no change in this nitrogen-partition. Interstitial nephritis, however, is characterized by a pronounced increase in the percentage of nitrogen as urea, and a decrease in the rest-nitrogen. The blood in eclampsia forms a marked contrast to this. In eclampsia there is a relative drop in the urea nitrogen, but a very marked increase in the rest-nitrogen. It will be observed also that the nitrogen in the uric acid forms a greater fraction of the nonprotein nitrogen than either in nephritis or gout. This marked increase in the rest-nitrogen of blood is of diagnostic value in the toxemias of preg-

nancy. The rest-nitrogen, however, can be determined only by subtracting from the total nonprotein nitrogen, the amount of nitrogen contained in the urea, the uric acid, and the creatinin. No variations have been noted in the concentration of amino-acids or ammonia, and for clinical purposes these factors need not be brought into consideration. Hence in eclamptic bloods it is essential to determine the nonprotein nitrogen in addition to the urea, uric acid and creatinin.

TABLE II

COMPARATIVE NITROGEN PARTITION OF BLOOD

In per cent of total nonprotein nitrogen

Blood	Uric Acid N	Urea N	Creat-inin N	Ammo-nia N	Rest N
Normal	2	50	2	0.3	46
In gout and early nephritis	6	50	2	0.3	42
In parenchymatous nephritis	2	55	2	0.3	40
In severe interstitial nephritis	2 to 3	75	2.5	0.5	20
Eclampsia	7.7	16	2	0.3	73

Uric Acid.—Urea is the nitrogenous waste product of the metabolism of simple proteins, but uric acid is derived from the metabolism of a group of conjugated proteins—the nucleins. The nucleins contain nucleic acid, which is split into its various constituents by endocellular enzymes—the nucleases. During this autolysis the purin bases are liberated from the other constituents of the nucleic acid molecule. These are then deamidized and oxidized by a group of enzymes to the final product—uric acid. The uric acid of the blood has a twofold origin. One portion arises from the disintegration of the nuclein material of the body tissue; the other portion is produced during the metabolism of the nucleins of the diet. The source of the uric acid then is both endogenous and exogenous. The concentration of this product in normal blood after an average mixed diet is from 2 to 3 milligrams per 100 cubic centimeters. A restriction of the purin intake will diminish the amount of uric acid in the blood possibly to 1 or 1.4 milligrams, while the ingestion of a diet rich in purin leads

to an increase of the uric acid in the blood. In gout the concentration of this product may rise to 6 milligrams, whereas the other nitrogenous waste products remain at their respective normal levels. The etiological factors producing this high uric acid in gout are not understood at the present time.

Retention of.—Myers and Fine have pointed out that the kidney during excretion normally concentrates the creatinin one hundred times, the urea eighty times, but the uric acid only twenty times. Hence of these nitrogenous waste products the creatinin is the easiest to eliminate and the uric acid the most difficult, with the urea standing in an intermediate position. The order of retention of these nitrogenous waste products, as a result of renal disease, will depend upon the comparative ease with which the kidney excretes them. A lowering of the permeability of the kidney in the initial stages of renal impairment leads to an accumulation of the uric acid in the blood. This retention of uric acid takes place long before there is any appreciable increase in the nonprotein and urea nitrogen or creatinin, and it is an earlier and more reliable indication of an insufficiency of kidney function than a proteinuria or cylinduria. Baumann, Hansman, Davis and Stevens, after a thorough study of tests of renal function in a large series of cases, have concluded that the rise in the concentration of uric acid in the blood is the most sensitive index of a failing kidney function at our disposal. Later, as the involvement of kidney function progresses, the urea accumulates in the blood, but in general there is no perceptible rise in the creatinin concentration until the urea nitrogen has been doubled or more than doubled.

Increase of.—From the data presented in Table III it is evident that in mild involvement of kidney function there is a definite increase in the uric acid, but the urea nitrogen and creatinin remain normal. In the moderately severe cases there is a retention of urea nitrogen in addition to the uric acid. The creatinin, however, remains fairly normal. A severe nephritis entails a definite increase in the creatinin in addition to the uric acid and urea nitrogen. The progressive steps in the involvement of the excretion of these nitrogenous waste products present a staircase effect.

Creatinin.—Creatinin is the anhydrid of creatin (methyl guanidin acetic acid), the chief nonprotein nitrogenous constituent of

TABLE III—Staircase Retention of Uric Acid, Urea and Creatinin in Nephritis *

Date 1915–1919	Case	Age	Sex	Diagnosis	Condition	Mg. per 100 c.c. of Blood			Phthalein 2 Hrs., Per cent	Systolic Blood Pressure	Urine	
						Uric Acid	Urea N	Creatinin			Albumin	Casts
I												
9/17	H. L.	23	♂	Pulmonary tuberculosis	Unchanged	6.5	16	2.7	58	130	++	+
8/10	E. H.	41	♂	Pericarditis	Unchanged	5.6	13	2.1	45	150	−	−
10/12	F. D.	45	♂	Interstitial nephritis	Unchanged	5.5	12	2.5	37	185	−	+
3/ 6	B. D.	35	♀	Diffuse nephritis	Unchanged	9.6	19	2.4	45	175	+	+
II												
8/11	J. J.	65	♂	Early interstitial nephritis	Unchanged	9.5	25	2.5	13	185	+	+
7/21	D. S.	56	♂	Early interstitial nephritis	Unchanged	6.6	24	3.3	26	185	−	+
9/21	D. D.	52	♂	Early interstitial nephritis	Unchanged	8.7	20	3.6	20	100	+	+
8/ 3	C. M.	54	♂	Early interstitial nephritis	Unchanged	6.3	31	2.0	23	150	−	−
III												
1/ 6	L. P.	57	♂	Moderately severe chronic inserstitial nephritis	Improved	8.0	80	4.8	0	240	++	++
3/ 1						4.9	17	2.9	10	170		
4/23	J. P.	34	♂	Moderately severe chronic diffuse nephritis...	Improved	8.3	72	3.2	25	238	+++	++
5/21						5.3	21	1.9	43	145		
1/15	W. C.	49	♂	Moderately severe chronic diffuse nephritis...	Improved	9.5	44	3.5	38	210	++	++
1/28						2.5	19	1.9	52	120		
IV												
4/11	E. C.	50	♀	Typical fatal case of chronic interstitial nephritis	Died	22.4	236	16.7	0	210	++	Pus
3/23	T. D.	34	♂	Typical fatal case of chronic interstitial nephritis	Died	15.0	240	20.5	2–3	225	++	+
1/25	S. H.	37	♂	Typical fatal case of chronic interstitial nephritis	Died	14.3	263	22.2	0	220	++	+
4/15	J. W.	34	♂	Typical fatal case of chronic interstitial nephritis	Died	8.7	144	11.0	Trace	225	+	+

* From Chace and Myers, 1916.

muscle. Folin first proved that the amount of creatinin excreted in the urine of a normal individual on a meat-free diet is independent of both the amount of protein in the food and of the total nitrogen of the urine. The creatinin, therefore, is not derived from the diet, but its source on a meat-free diet is entirely endogenous. The relation of the creatinin excreted to the creatin content of the muscles has long been a disputed question. The evidence presented by Myers and Fine supports the view that the creatinin is formed in the muscle tissue from creatin at a very constant rate. While all muscles have the property of producing creatin and converting it into creatinin, it is certain that muscular work does not increase creatinin production. Creatin probably is evolved and converted into creatinin in the formative metabolism of muscles rather than during muscular contractions. The creatinin is then a product of the "wear and tear" of the tissues rather than of any special function.

Of all the tissues of the body, the kidneys contain the greatest amount of creatinin, next in order come the muscles and then the blood. This would indicate that after its formation in the muscles the creatinin is transported by the blood to the kidney for excretion. Myers and Fine have found in a case of uremia a creatinin content of the blood slightly exceeding that of the muscles. For normal individuals the creatinin of the blood amounts to from 1 to 2 milligrams per 100 cubic centimeters. The fact that creatinin is entirely of endogenous origin and is readily eliminated by the kidneys renders it an excellent prognostic index of renal function. In miscellaneous pathological conditions uncomplicated by renal involvement values below 2.5 milligrams per 100 cubic centimeters are obtained. In syphilis, some cardiac conditions, and occasionally in fevers and advanced diabetes, between 3 and 4 milligrams are found. An accumulation of the creatinin to 3.5 milligrams, or more, indicates a severe disturbance of kidney function. Myers and Killian have shown that some cases with creatinin values below 4 milligrams show improvement, but almost invariably a fatal termination from the kidney damage results when the creatinin rises to more than 4 milligrams per 100 cubic centimeters. A retention of creatinin to this extent indicates a severe impairment of renal function.

Chlorids.—The description of a simplified technic for the determination of the chlorids of the blood by Myers and Short

has made it possible to include this estimation in our chemical analyses of the blood for clinical purposes. Some workers have confined their studies to the chlorids of the whole blood, and others to chlorids of the plasma or serum. Normally the total chlorids of the whole blood (determined as NaCl) range from 0.45 to 0.50 per cent, but the chlorids of the plasma are about 0.12 per cent higher. Since the tissues of the body come into intimate contact with the blood plasma rather than the whole blood, it is logical to expect that changes in the chlorid content of the tissues would be more significantly reflected in similar variations in blood plasma. However, on standing, or upon shaking, there is an escape of CO_2 from the blood, which produces a passage of chlorids from the cells into the plasma. This increases the chlorid content of the plasma but does not affect the chlorids of the whole blood. Hence determinations made upon the whole blood are more trustworthy than those upon the plasma.

The excretion of chlorids and nitrogen appear to be independent functions on the part of the kidneys. In nephritis of the interstitial type the excretion of nitrogen is markedly impaired, but the excretion of chlorids is fairly normal. Here when high blood chlorids are found, a restriction of the chlorid intake quickly restores them to normal. However, the restriction of the chlorid intake must always be gauged by the level of the blood chlorids. In parenchymatous nephritis, on the contrary, the nitrogen retention is comparatively small, but there is diminished excretion of chlorids. This retention of chlorids is accompanied by an edema, and the blood chlorids gradually return to normal with the subsidence of the edema. Allen has recently endeavored to establish a causative relation between the retention of chlorids in the plasma and the development of hypertension simplex, and hypertension in renal disease. Subsequent experimental studies on the part of other workers have failed to confirm Allen's contention. Furthermore, our studies on toxemias of pregnancy have shown that in these conditions there is no definite relation between the level of the blood chlorids and the hypertension, but that the appearance of the edema was paralleled by a significant rise in the chlorids of the whole blood. Apparently a deficiency of chlorid excretion is a causative factor in producing this edema, and a limitation of the chlorid intake, guided by the level of the blood chlorids, leads to a diminution of the edema. In cases manifesting

edema, the value of the estimation of the blood chlorids for the guidance of treatment cannot be overemphasized.

The sugar concentration of normal blood after a fast of from 12 to 14 hours is 0.09 to 0.12 per cent. However, after a meal rich in carbohydrate, there may be an appreciable rise in the blood-sugar to 0.13 or 0.14 per cent. Blood-sugar concentrations exceeding 0.12 per cent are termed hyperglycemias, and less than 0.09 per cent hypoglycemias. Hypoglycemias are found in conditions resulting from a hypo-endocrin function, for example, myxedema, cretinism, Addison's disease and also in muscular dystrophy. Hyperglycemias are more commonly encountered, for example, in diabetes, nephritis and hyperthyroidism. Myers and Killian have shown that the hyperglycemia in nephritis, diabetes and hyperthyroidism is dependent upon an increased diastatic activity of the blood. The increased diastatic activity in nephritis finds an explanation in diminished excretion of this enzyme in the urine. The mechanism of the production of the hyperactivity of the diastase in the blood in diabetes is still an obscure point. However, a hyperfunction of the ductless glands, particularly of the thyroid, appears to result in an increased diastatic activity and a hyperglycemia. The author has noted a parallelism between the alkali reserve and the diastatic activity of the blood. An increase in the alkali reserves inhibits the diastatic activity, whereas a decrease in the alkali reserve provokes an increased activity. The hyperglycemias noted in the toxemia of pregnancy find a possible explanation in the variations in the diastatic activity of the blood.

Alkali Reserve.—During health the blood is constantly maintained at a slightly alkaline reaction through the medium of its bicarbonates, phosphates and proteins. These compounds constitute the alkali reserve of the blood. A diminution of this alkali reserve is commonly called an acidosis, although this term is somewhat misleading, since the blood never during life becomes acid in reaction. Acidosis may be produced either by an abnormal formation of acid substances, or it may be due to an inability to remove from the body acid compounds normally present in the blood. The kidneys excrete an acid urine from a fairly neutral blood. The acidity of the urine is largely due to excess of acid phosphates over alkaline phosphates. This removal of acid phosphates by the kidneys is one means of maintaining the alkali

reserve of the blood. In nephritis the kidneys may lose the power to eliminate these compounds, and this failure to excrete them gives rise to a predominance of the acid phosphates over the alkaline phosphates, thus depleting the alkali reserve of the blood. Marriott and Howland have demonstrated an increase in the inorganic phosphates in the blood plasma in nephritis with acidosis, but no increase was noted in nephritis unaccompanied by acidosis. The acidosis of nephritis is then due, not to an abnormal production of acid bodies, but rather to the accumulation of acid phosphates which the kidneys fail to remove. It is important to note that the acidosis of nephritis is not accompanied by a ketosis (acetonuria), and the only reliable method of detecting or estimating this acidosis is by determining the alkali reserve of the blood.

The defective oxidation of the fats in diabetes leads to the production of the acetone bodies—acetone, diacetic acid and β-oxybutyric acid. The neutralization of these compounds by the sodium bicarbonate of the blood plasma results in the taking up of the sodium by the organic acids and a liberation of the carbon dioxid. In this manner the body is robbed of its alkali reserve. In the eclamptic toxemias and in pernicious vomiting a very marked decrease in the alkali reserve has been found. There can be no doubt that the acidosis in pernicious vomiting is a type of starvation acidosis due to production of abnormal acid bodies in faulty metabolism. In the eclamptic toxemias the repeated tonic muscular contractions result in the formation of such acid bodies as lactic acid and acid phosphates. There is also the additional acid production due to the starvation. Zweifel isolated sarcolactic acid in considerable quantities from the maternal venous blood and the blood of the cord. He ascribed the eclamptic toxemias to an acid intoxication. Although it is now definitely known that the acidosis is the effect rather than the cause of the toxemia, a knowledge of the extent of this acidosis is of prime importance from a therapeutic standpoint.

The body is able to handle quite large quantities of acids without a drop in the alkali reserve. The increased carbon dioxid tension of the blood plasma, due to the liberation of carbon dioxid from the bicarbonates in the neutralization of the acids, incites an increase of pulmonary ventilation. In this manner the carbon dioxid is removed at a rapid rate. The acetone bodies are elim-

inated in the urine producing a ketosis (acetonuria). An abnormal formation of ammonia takes place from the amino groups split off from the amino acids, and this serves to neutralize a portion of the organic acids. The increased production of the ammonia is at the expense of the urea. Finally, the proteins may react as bases and take up considerable quantities of the acids without a perceptible change in their reaction. If the acid bodies are neutralized and eliminated without producing a diminution of the alkali reserve of the blood plasma, this condition is termed a compensated acidosis. However, when a decrease in the alkali reserve follows the acid intoxication, the acidosis is said to be uncompensated. A compensated acidosis is frequently noted during the last months of normal pregnancy.

Obviously the occurrence of acetone bodies in the urine indicates an abnormal acid production, but it tells us nothing concerning the extent of the acidosis. Moreover, in nephritic acidosis and in the nephritic toxemias, a ketosis is uniformly absent. In like manner no reliance can be placed upon the amount of ammonia excreted, or the ammonia coefficient, for these factors bear no definite relation to the decrease of the alkali reserve of the blood. A determination of the carbon dioxid tension in the alveolar air by the simple method of Marriott readily lends itself to clinical work. When the determinations are made with care, the results furnish a fair index of the acidosis. However, in cases of increased pulmonary ventilation, a lowered tension of carbon dioxid in the expired air will be noted, although no uncompensated acidosis exists. The depletion of the alkali reserve of the blood may be roughly determined by the Sellards method of alkali tolerance. This procedure has been adopted by White in a study of acidosis associated with the toxemias of pregnancy. Normally from 5 to 10 grams of sodium bicarbonate are sufficient to render the urine alkaline. In acidosis greater quantities of the alkali are required, in some cases as high as 100 grams. Palmer and Van Slyke have found that in many pathological cases the urine did not become alkaline until the plasma bicarbonate had been increased above that present in normal individuals. This gives not only an exaggerated conception of the acidosis, but also necessitates the administration of alkali in quantities sufficient to prove injurious.

Carbon Dioxid, How Determined.—Van Slyke has introduced a comparatively simple method of determining the carbon dioxid combining of the blood plasma as a measure of its alkali reserve. This method has been almost universally adopted in clinical laboratories. For a detailed description of the technic employed, reference may be made to Myers' work or to the original paper of Van Slyke and Cullen. The procedure consists in measuring the reserve alkali by determining the amount of carbon dioxid it can hold in combination, just as in gastric analyses the acid concentration is estimated in terms of the amount of alkali that will combine with it. The table below gives the range of finding for normal blood and the principal stages of acidosis.

TABLE IV

THE CO_2 COMBINING POWER OF BLOOD PLASMA IN NORMAL SUBJECTS AND IN ACIDOSIS *

Condition of Subject	CO_2 Combining Power of Plasma, c.c. per 100
Normal resting adult. Extreme limits.....	77–53
Mild acidosis, no visible symptoms.....	53–40
Severe acidosis, symptoms of acid intoxication.	Below 31
Lowest CO_2 observed, with recovery.....	16

The etiological factors producing the acidosis may vary, but the effect is the same in all cases, that is, a lowering of the alkali reserve of the blood. Hence the carbon-dioxid combining power of the blood plasma is a reliable index of all types of acidosis.

NORMAL PREGNANCY

Blood Changes in.—Studies on 5 cases of normal pregnancy are presented in Table V. The nonprotein nitrogen is at a low normal level, or slightly decreased (21 to 25 milligrams), and corresponding to this there is a proportionate diminution in the urea nitrogen (9 to 11 milligrams). The relation of the urea nitrogen to the nonprotein nitrogen furnishes a reliable estimate of the rest-nitrogen. In normal pregnancy the urea nitrogen forms about 44 per cent of the nonprotein nitrogen, slightly less than in

normal nonpregnant cases. The figures for uric acid, creatinin, and chlorids are well within normal limits. With the exception of cases 1 and 2, normal blood-sugars have been found. In these cases slight hyperglycemias were noted. A definite decrease in the carbon dioxid combining power of the blood plasma was found to be the rule in the last months of normal pregnancy. The maximum decrease was to 39 volumes per cent. This drop in the alkali reserve was not associated with a ketosis, but was found to be associated with mild symptoms of dyspnea after physical exertion. It is evident from these findings, and also from the works of Hasselbach and Gammeltoft, of Losee and Van Slyke, and of White and Emge that a mild acidosis prevails during the last months of pregnancy.

TABLE V

COMPOSITION OF THE BLOOD IN NORMAL PREGNANCY

Case	Age	Para	Mos. of Gest.	Blood Analyses							
				Non-protein N	Urea N	Urea N / N–P–N Per cent	Uric Acid	Creatinin	Sugar	Chlorids	CO_2 Combining Power
				Mg. per 100 c.c.			Mg. per 100 c.c.		Per cent		
1. A. P.	20	I	5	25	11	42	2.0	2.3	0.13	0.48	
2. N. C.	25	I	7½	25	11	45	2.6	2.1	0.14	0.46	42
3. A. S.	23	I	8	24	11	47	2.6	2.5	0.10	0.48	49
4. E. Q.	27	I	8	22	10	44	2.5	2.4	0.11	0.48	44
5. M. N.	33	III	8	21	9	44	1.9	2.0	0.10	0.48	39

NEPHRITIC TOXEMIAS

Blood Changes in.—The group of nephritic toxemias embraces those cases that in their previous histories and in many of their clinical findings present evidence of a preëxisting impairment of kidney function, either acute or an exacerbation of a chronic condition. The renal insufficiency is not consequent to the toxemia, but, on the contrary, it may have been a predisposing cause

TABLE VI

CHEMICAL CHANGES IN THE BLOOD IN THE NEPHRITIC TOXEMIAS

Case	Age	Para	Mos. of Gest.	Blood Analyses								Remarks
				Non-protein N	Urea N	Urea N / N-P-N Per Cent	Uric Acid	Creatinin	Sugar	Chlorids	CO_2 Combining Power	
				Mg. per 100 c.c.			Mg. per 100 c.c.		Per Cent			
1. N. C.	45	X	7	189	111	60	18	17.6	0.20	0.52	22	Neuroretinitis. Convulsions. Stillbirth. Died after cesarean section
2. C. Q.	27	III	6½	106	72	67	8.1	3.7	0.12	0.42	40	Neuroretinitis. No edema. Delivered by bag. Improvement slight
3. N. K.	27	II	5	47	25	53	..	2.2	0.10	..	..	Convulsions. No edema. Cesarean. Fetus dead
4. C. C.	32	III	7½	46	26	57	..	..	0.14	0.50	..	Neuroretinitis. Convulsions. Slight improvement after cesarean
5. A. P.	33	II	8	45	28	62	4.8	2.8	0.12	0.47	43	Neuroretinitis. No edema. Convulsions. Delivered by forceps. Improvement slight
6 B. G.	36	III	8	32	14	44	5.1	3.0	0.09	0.55	..	Marked edema. No convulsions. Slight improvement after cesarean
7. M. C.	35	IV	7	29	15	51	5.3	2.6	0.14	0.52	..	Marked edema. Neuroretinitis. No convulsions. Cesarean. Improved

toward the development of the toxemia. Seven cases are reported in Table VI. The first five show a marked impairment of nitrogen elimination. A comparison of these findings with those in Tables II and III demonstrates that the changes observed in the blood of these cases are in accord with the variations typical of moderate or severe renal impairment in general. The nonprotein nitrogen is greatly increased (45 to 189 milligrams), but the characteristic feature of these cases is that the urea nitrogen constitutes a larger fraction of the nonprotein nitrogen than in normal blood. Such is also the case in nonpregnant nephritics. The retention of uric acid is quite marked, but there is no very appreciable increase in the creatinin except in the first 2 cases. Case 1 died about forty-eight hours after delivery. The creatinin here rose to 17.6 milligrams. All of these patients were eclamptics, and not merely cases of nephritis complicating pregnancy. It is inconceivable that such an extreme damage to kidney function as that presented in Case 1 could develop from a toxemia within twenty-four to forty-eight hours, as Caldwell and Lyle maintain. There must have been some previous kidney damage which favored the development of the toxemia. Following the evacuation of the uterus, there is but little improvement in these cases and the chemical changes in the blood point to a more or less permanent disturbance of kidney function.

Another type of toxemia of renal origin is represented by the last 2 cases. The urea and nonprotein nitrogen do not vary from the normal, but the uric acid is definitely increased (5.1 to 5.2 milligrams). The chlorid concentration of the blood was found to be 0.52 and 0.55 per cent. These high blood chlorids in spite of a salt-free diet were coincident with a pronounced general anasarca which had been progressing for some time previous to the patient's admission to the hospital. The output of urine was scanty and it contained a large amount of protein. These findings indicate a definite impairment of chlorid excretion with but little involvement of nitrogen. These 2 cases at no time had convulsions, but they did complain of pronounced visual disturbances accompanied by nausea and headache. After emptying the uterus and giving medical treatment to increase salt elimination, the subsidence of the edema was antedated by a decrease in the blood chlorids. In this type of case, the variations in the blood chlorids

are of the greatest value from a prognostic and therapeutic standpoint.

We may now discuss the blood pictures in the various types of toxemia according to the classification adopted in the section on Etiology.

ACUTE YELLOW ATROPHY OF THE LIVER

Blood Changes in.—In acute yellow atrophy of the liver there is a complete, or almost complete, loss of function of this organ, with little or no impairment of the functions of other organs. Van Slyke and Stadie have reported fairly complete chemical studies upon the blood and urine in a case of acute yellow atrophy. Of the total nitrogen excreted in the urine (twenty-four hours before death) about 52 per cent was in the form of urea, 17 per cent as ammonia, and 16 per cent as amino-acids. The output of the urea nitrogen was diminished, but both the ammonia and amino-acid nitrogen were very markedly increased. The urea nitrogen of the blood remained within normal limits, but the amino-acid nitrogen was from two to three times the normal figure. A decrease in the alkali reserve of the blood was also noted. An examination of the nitrogen content of the liver in this case demonstrated an amino-acid and peptid nitrogen content about three times as great as that found in normal dogs' livers. These results point to the conclusion that in acute yellow atrophy the proteins of the liver are autolyzed at a rapid rate into peptids and amino-acids. In the normal human organism from 85 to 95 per cent of the amino-acid nitrogen is converted into urea, the amino-acid nitrogen constituting but 4 to 8 milligrams per 100 cubic centimeters of the blood, and but 2 per cent of the total nitrogen of the urine. However, in the case studied by Van Slyke and Stadie, only 60 per cent of the amino-acid nitrogen was transformed into urea, and the amino-acid nitrogen of the urine rose to 16 per cent of the total nitrogen. Acute yellow atrophy, with the possible exception of fatal phosphorus poisoning, is the only clinical condition in which abnormal quantities of amino-acids are found in the blood and urine.

One case of acute yellow atrophy has come under the observation of the author. During the fifty hours of the patient's stay in

the hospital there was persistent nausea and vomiting and a pronounced jaundice. A post-mortem examination confirmed the diagnosis. A specimen of blood was obtained about thirty hours before death which was found to contain 80 milligrams of nonprotein nitrogen, 27 milligrams of urea nitrogen, and 14.5 milligrams of uric acid. The urea nitrogen here forms 33 per cent of the nonprotein nitrogen. The amino-acid nitrogen was not determined, but it is evident that there is a significant increase in the rest-nitrogen. In this case, the increase in the urea nitrogen and of the uric acid must be attributed to a secondary involvement of kidney function as well as to protein autolysis. The increase in the rest-nitrogen observed in this case is somewhat similar to that found in eclampsia; however, the factors causing this increase in the nonprotein nitrogen appear to be different in the two conditions. Despite the marked degenerative changes that occur in the liver in the toxemias of pregnancy, Losee and Van Slyke have found no increase in the amino-acid nitrogen of the blood or urine.

HYPEREMESIS

Blood, Changes in.—In Table VII are presented findings in typical cases of hyperemesis. The nonprotein nitrogen is definitely increased above the normal (34 to 65 milligrams); with the exception of case 5, the urea nitrogen is normal or slightly decreased. It is evident that since in these cases the urea nitrogen forms a low fraction of the nonprotein nitrogen (from 15 to 31 per cent) the rest-nitrogen must be proportionately increased. In case 5, although there is a moderate retention of urea nitrogen amounting to 27 milligrams, it forms only 41 per cent of the nonprotein nitrogen. Here there is a marked impairment of kidney function, but, as in many cases to be discussed later, this renal impairment is secondary to the toxemia. Cases of hyperemesis are characterized by an increase in the nonprotein nitrogen with an abnormally small fraction in the form of urea. It will be noted that these patients also show an increased uric acid; however, the increase in the concentration of this product is not so great as that noted in eclampsia. No disturbance of the creatinin, sugar or chlorids has been observed.

Carbon Dioxid Combining Power, Decrease of.—A decrease in the carbon dioxid combining power of the blood plasma was

TABLE VII

CHEMICAL CHANGES IN THE BLOOD IN HYPEREMESIS

Case	Age	Para	Mos. of Gest.	Blood Analyses								Remarks
				Non-protein N	Urea N	Urea N / N–P–N Per Cent	Uric Acid	Creatinin	Chlorids	Sugar	CO_2 Combining Power	
				Mg. per 100 c.c.			Mg. per 100 c.c.		Per Cent			
1. C. B.	22	I	3	34	12	33	3.0	1.9	0.47	0.12	28	No convulsions. Duration 3 weeks
2. L. S.	20	I	4	35	11	31	5.0	1.7	..	0.12	36	No convulsions. Duration 2½ weeks
3. D. M.	22	I	3	46	14	30	..	..	..	0.11	..	No convulsions. Duration 1 week
4. N. B.	19	II	3	56	8	15	..	1.6	0.41	0.14	42	Previous pregnancy also toxic. Duration 1 week. No convulsions
5. N. B.	23	I	3	65	27	41	6.1	..	..	0.10	46	Duration 6 days. No convulsions

invariably noted in our cases. The figures reported range from 28 to 46. Hyperemesis is then associated with a more or less severe acidosis. Emge has found a carbon dioxid combining power of the blood plasma from 35 to 46 in the excessive vomiting of pregnancy. In the cases of pernicious vomiting reported by Losee and Van Slyke there is a decrease in the alkali reserve of the blood, but it is not greater than that observed in normal pregnancy. In following the progress of the toxemia it has been noted that the depression of the carbon dioxid combining power of the blood follows the rise in the nonprotein nitrogen and the appearance of the clinical symptoms of the toxemia. The acidosis is not an etiological factor in the production of the hyperemesis, but, on the contrary, appears to be dependent on the severity and duration of the nausea and vomiting. A somewhat similar conclusion has been reached by Underhill and Rand in their studies on the ammonia excretion in the urine. These authors have pointed out that the composition of the urine in pernicious vomiting is strikingly similar to that found in inanition. The acidosis, gauged by the ammonia excretion, is promptly relieved by the administration of carbohydrate by mouth or by rectum. The acidosis of hyperemesis appears to be a type of starvation acidosis. Although this acidosis is the effect, rather than the cause, of the toxemia, from a therapeutic standpoint a knowledge of any change in the alkali reserve of the blood is of great value. Despite the fact that both Joslin and Allen are opposed to the extensive use of sodium bicarbonate in acidosis, the administration of this alkali has been generally accepted as the most efficient means of combating an acidosis. However, Palmer and Van Slyke advise the careful control of the amount of the alkali used. These authors have found that for each forty-two pounds of body weight 0.5 gram of sodium bicarbonate will raise the carbon dioxid combining power 1 per cent by volume. The practical value of a knowledge of the carbon dioxid combining power of the blood can well be illustrated by case 1. Here an evacuation of the uterus to relieve the hyperemesis was decided upon, but since anesthesia and operative procedure decrease the alkali reserve of the blood, it is essential first to relieve the existing acidosis. The carbon dioxid combining power must be raised from 28 to 60, that is, 32 volumes per cent. The body weight was one hundred and two pounds, that is 2.4 times Van Slyke's unit (forty-two pounds). The

dose of sodium bicarbonate required in this case to restore the normal alkali reserve of the blood was calculated as follows: $0.5 \times 2.4 \times 32 = 38.4$ grams. The sodium bicarbonate was given intravenously in enough water to make a 4 per cent solution. This amount of alkali is sufficient to replenish the alkali reserve of the blood, but to maintain it within normal limits, bicarbonate in a 2 per cent solution was administered by rectum after operation until all symptoms of the toxemia had disappeared.

PRE-ECLAMPSIAS AND ECLAMPSIAS

Blood Change in.—In Table VIII cases 1 and 2 are pre-eclampsias, the following 5 cases are post-partum eclampsias, and the remaining cases are ante-partum eclampsias. Although the term "hepatic toxemia" has frequently been applied by some clinicians to this type of pregnancy toxemia, we have no proof that this condition is of hepatic origin. Inspection of the table discloses that the nonprotein nitrogen is invariably above the high normal limit, and in some instances more than double this figure. The values found range from 29 to 94 milligrams. In the pre-eclampsias the increase in the nonprotein nitrogen is not so great as in the true eclampsias. With the exception of the last 4 cases, the urea nitrogen is at the low normal level or markedly decreased; values from 5 to 14 milligrams being obtained. A remarkably low percentage of the nonprotein nitrogen is in the form of urea. The highest percentage found was 38 and the lowest 15.

High Nonprotein Nitrogen.—We believe that the high nonprotein nitrogen, of which the urea nitrogen forms a small percentage, is characteristic of the pregnancy toxemias of this type. This low ratio of the urea nitrogen to the nonprotein nitrogen indicates a marked increase in the rest-nitrogen. The increase in the rest-nitrogen cannot be explained by a rise in the amino-acid nitrogen. In a series of 23 cases of toxemias studied by Van Slyke and Losee the amino-acid nitrogen of the urine did not exceed 3.6 per cent, the maximum found in the urine of normal men. The blood of 10 eclamptic women gave figures for the amino-acid nitrogen within 4 to 8 milligrams, the normal established by Ellis, Cullen and Van Slyke. The high rest-nitrogen

with a normal amino-acid nitrogen characterizes the eclamptic patient but a high rest-nitrogen with an increased amino-acid nitrogen is found only in acute yellow atrophy of the liver.

Urea and Rest-nitrogen.—The high nonprotein and the low urea nitrogen of the blood in eclampsia form a significant contrast to the findings for these products in the blood in nephritic toxemias. In nephritic toxemias the nonprotein nitrogen is increased, but there is proportionately a greater rise in the urea nitrogen, so that the urea nitrogen forms more than 50 per cent of the nonprotein nitrogen. It has been our experience that the increase in the rest-nitrogen of the blood in eclampsia (judged by the relation of the urea to the nonprotein nitrogen) bears a somewhat definite relation to the extent of the toxemia. In the preeclampsias there is a beginning increase in the nonprotein nitrogen, the ratio of the urea to the nonprotein nitrogen being slightly less than in normal pregnancy. In the eclampsias, however, at the height of the toxic state the rise in the nonprotein nitrogen is very marked, and the ratio of the urea nitrogen to it is relatively decreased. Moreover, the toxemia is relieved by therapeutic measures, and the subsidence of the toxemia is preceded by a drop in the nonprotein nitrogen. Apparently, the factor causing the toxemia is a component of this increased rest-nitrogen, but its nature and origin are still matters of speculation.

Uric Acid Concentration.—The increase in the concentration of uric acid is very marked and, we are convinced, particularly significant. It will be noted that the uric acid figures vary from 3 to 11 milligrams. Slemons and Bogert obtained normal figures for uric acid in the blood in uncomplicated pregnancy, but in preeclampsia, eclampsia and nephritis complicating pregnancy, values from 6 to 9 milligrams were obtained. Caldwell and Lyle have reported an average figure of 6.2 milligrams for the uric acid of the blood in pregnancy toxemias and eclampsias. Slemons and Bogert have noted an increase in the uric acid content of the blood at the end of labor, and this increase was more pronounced in primiparæ than in multiparæ. These authors have suggested that the muscular contractions during labor might increase the production of endogenous uric acid. In a similar manner the convulsions in eclampsia would give rise to a high uric acid content of the blood. Such, however, is not the case. Uric acid is not derived from muscular activity. It has been noted by Killian and

TABLE VIII

CHEMICAL CHANGES IN THE BLOOD IN PRE-ECLAMPSIA AND ECLAMPSIA

Case	Age	Para	Mos. of Gest.	Blood Analyses								Remarks
				Non-protein N	Urea N	Urea N / N–P–N Per Cent	Uric Acid	Creatinin	Sugar	Chlorids	CO_2 Combining Power	
				Mg. per 100 c.c.			Mg. per 100 c.c.		Per Cent			
1. M. P.	22	I	5½	29	11	37	3.1	1.9	0.12	..	52	Pre-eclampsia
2. M. Z.	20	I	7	41	18	43	9.0	..	0.12	..	49	Pre-eclampsia
3. B. W.	25	I	9	30	5	16	8.5	..	0.10	0.63	16	Convulsions began 3 hours post partum
4. M. B.	21	I	9	36	11	32	4.8	1.9	0.15	..	..	Convulsions began 1 hour post partum
5. J. H.	20	I	9	37	10	27	3.8	..	0.09	0.59	42	Convulsions began 2 days post partum
6. H. S.	22	I	9	48 26	15 13	32 50	7.3 3.5	1.8 2.1	0.13 0.12	0.46 0.50	28 40	Convulsions began 2 hours post partum 14 days later. Improved
7. L. T.	33	II	9	58	11	17	4.3	..	..	..	..	Convulsions began 1 hour post partum
8. M. E.	27	I	7	34	13	36	11.0	2.5	0.13	..	38	Severe convulsions. Stillbirth. Died from post operative acidosis
9. Y. H.	28	I	7½	35 23	9 12	27 51	6.8 2.5	.. ..	0.12 0.09	.. ..	38 53	Severe convulsions. Stillbirth 5 days later. Improved

10. M. B.	29	III	9	36	9	22	4.5	1.9	0.12	0.52	26	Convulsions. Edema. Stillbirth
11. B. R.	33	I	9	36	12	34	3.6	1.7	0.17	0.47	34	Mild convulsions. Fetus toxic
12. H. B.	32	III	7	37	14	34	6.5	..	0.10	0.58	40	Severe convulsions. Stillbirth
13. D. M.	22	I	8	37	11	29	5.0	..	0.14	0.47	37	Severe convulsions. Fetus toxic
14. F. H.	27	I	7	38	10	29	3.4	..	0.10	0.61	12	Severe convulsions. Edema. Died from post operative acidosis
15. E. R.	32	I	7½	39	12	30	7.5	2.3	0.13	0.47	40	Severe convulsions. Stillbirth.
16. R. W.	24	II	8	40	6	16	6.8	2.5	0.13	0.55	36	Severe convulsions. Slight edema. Stillbirth
17. E. P.	20	I	7½	40	6	16	6.9	2.2	0.12	0.52	30	Severe convulsions. Slight edema. Stillbirth
18. N. L.	24	II	7	47	14	29	5.4	..	0.12	0.63	..	Severe convulsions. Marked edema. Stillbirth
19. A. B.	21	I	9	50	9	18	5.6	2.2	0.18	0.52	21	Severe convulsions. Fetus toxic
20. S. B.	29	IV	9	52 20	9 9	17 45	8.5 2.1	3.4 2.2	0.30 0.12	.. ..	10 48	Diastatic activity = 28. Severe convulsions Diastatic activity = 16. Improved after 14 days
21. S. M.	30	II	7	54	22	42	6.5	2.0	0.13	..	33	Moderate convulsions. Stillbirth
22. A. C.	18	I	5	64 90	18 43	28 47	6.8 3.2	1.7 3.7	0.12 ..	0.50 0.61	26 52	Very severe convulsions. Stillbirth 8 days later. Marked edema. Died.
23. M. R.	21	I	7	56	22	38	6.5	2.7	0.11	0.52	20	Very severe convulsions. Stillbirth
24. B. S.	26	I	6½	64	22	32	8.6	2.5	0.10	0.42	..	Very severe convulsions. Stillbirth

Sherwin that the increase in the uric acid content of the blood in eclampsia is accompanied by other evidences of renal impairment, for example, by proteinuria and cylindruria. There can be no question but that this increase in the concentration of uric acid must be attributed to a mild involvement of kidney function consequent to the toxemia. A determination of the uric acid of the blood does not help to differentiate the types of pregnancy toxemias, but as an index of an early disturbance of kidney function its value cannot be overestimated.

It will be noted that in the last 4 cases the urea nitrogen has been increased above the upper normal level (18 to 22 milligrams). Kast and Wardell have concluded as a result of careful studies on the significance of the concentration of the urea nitrogen in the blood in various conditions, that values of 20 milligrams or more have a pathological significance. The only factor capable of producing an increase of the urea nitrogen of the blood is disturbance of kidney function. It is indeed true that an increase in exogenous protein metabolism entails a greater production of urea, but with normal kidney function an increased elimination of urea results so that the urea nitrogen of the blood is maintained within normal limits. The impairment of the functioning power of the kidneys has advanced in these last 4 cases so far that it not only inhibits the excretion of uric acid, but also that of the urea. However, it is significant that in these cases, although there is a retention of urea, the urea nitrogen of the blood continues to form only a small percentage of the nonprotein nitrogen. A comparison of these figures with those for the nephritic toxemias demonstrates that the actual amounts of nonprotein and urea nitrogen in themselves are of no value in differentiating the types of toxemia, but the ratio of the urea nitrogen to the nonprotein is characteristic for each type.

The statement of Ewing and Wolf that persistent toxemia tends to involve the kidneys progressively is confirmed by the observations on case 20. In the ante-partum specimen of blood, obtained when convulsions lasting from three to four minutes were rapidly succeeding one another, the nonprotein nitrogen was found to be 64 milligrams, the urea nitrogen 18 milligrams, the uric acid 7.5 milligrams, and the creatinin 1.7 milligrams, the urea nitrogen constituting only 28 per cent of the nonprotein nitrogen. The convulsions ceased after the evacuation of the uterus, but

otherwise there was no improvement. The patient continued in a semicomatose state, general edema developed and there was but a slight drop in the blood pressure. Another specimen of blood was obtained eight days after parturition when the patient appeared to be in a critical condition. There were, however, no convulsions. At this time the nonprotein nitrogen had risen to 90 milligrams, the urea nitrogen to 43 milligrams, the uric acid had dropped to 3.2 milligrams, but the concentration of creatinin was increased to 3.7 milligrams. It is pertinent to note that in this second specimen of blood the urea nitrogen forms a much larger portion of the nonprotein nitrogen than in the ante-partum specimen. At the height of the toxemia the increase in the rest-nitrogen had reached its maximum. The disturbance of kidney function which was indicated by the increased uric acid in the ante-partum blood had progressed, in spite of the termination of the pregnancy to such an extent that a marked retention of urea and a mild accumulation of creatinin resulted. The order of retention of these nitrogenous waste products in cases of renal impairment consequent to the toxemias of pregnancy is in close accord with that frequently described by Myers and his coworkers.

Creatinin and Chlorids.—No variation from the normal was noted in the concentration of the blood creatinin. In some instances there was a definite increase in the chlorids of the blood. In cases 3 and 18 the chlorids rose to 0.63 per cent, in 12 to 0.58 per cent, and in 16 to 0.55 per cent. This rise in the blood chlorids was found to be associated with a more or less pronounced edema. No apparent relation between the level of the blood chlorids and the hypertension could be determined. In case 24 the blood-pressure rose to 210/110, although the chlorids were 0.42 per cent, while in case 16 the blood-pressure was 164/100, and the chlorids were increased to 0.55 per cent. Case 3 had a blood-pressure of 165/100 and a chlorid concentration of 0.63 per cent. A study of the progress of the toxemias has demonstrated that the rise in the blood-pressure appears almost as early in the course of the toxic state as the increase in the nonprotein nitrogen. However, a change in the concentration of the chlorids of the blood appears late in development of the toxemia, and apparently is due to a disturbance of cardiac or renal function. Moreover, in case 6 at the height of the toxemia the blood-pressure was 190/100, and the chlorids 0.46 per cent. After the

disappearance of the toxemia the blood-pressure had dropped to 100/65, but the chlorids rose to 0.50 per cent. Allen's explanation of hypertension is not confirmed by these studies upon the toxemias of pregnancy.

Hyperglycemia.—A mild hyperglycemia has been frequently noted in eclampsia. Morris has shown that a rise in the blood-sugar is evident after convulsions in the eclamptic toxemias. Since the specimens of blood studied by us were obtained during the convulsive period, the hyperglycemias may be attributed to this factor. In only one instance, case 20, was the diastatic activity of the blood determined. Here a blood-sugar of 0.30 per cent with a diastatic activity of 28 was found with a carbon dioxid combining power of 10. Two weeks later when the recovery was complete, the blood-sugar had dropped to 0.12 per cent, the diastatic activity to 16 and the carbon dioxid combining power had risen to 48. This patient gave no history of diabetes previous to the toxemia, and since leaving the hospital there has been no evidence of a glycosuria. Killian has shown that in diabetes a decrease in the alkali reserve of the blood provokes an increased diastatic activity and a corresponding hyperglycemia, whereas a rise in the alkali reserve inhibits the diastatic activity with a consequent drop in the blood-sugar. In a similar manner, variations in the diastatic activity of the blood may be found to be the cause of the hyperglycemias in eclampsia. This point, however, requires further corroboration.

In the eclampsias the decrease in the carbon dioxid combining power (42 to 10 volumes per cent) is particularly striking, indicating in most cases a severe acidosis. In this particular the cases of hyperemesis and eclampsia differ markedly from the nephritic toxemias. As in hyperemesis, this acidosis of eclampsia is consequent to the toxemia and a relief of the toxemia provokes a rise in the alkali reserve of the blood. The findings in case 22 are of interest in this connection. Here, during the eclamptic period, the carbon dioxid combining power had dropped to 26, but in the fatal nephritis following the toxemia, the carbon dioxid combining power rose to 52. At this time, however, there were no convulsions. It will be observed that the acidosis in the eclampsia is much greater than in hyperemesis or in pre-eclampsia. Another factor in addition to the starvation may be the cause of the acidosis in eclampsia. In general, it may be said that the greatest

decrease in the carbon dioxid combining power is found in those cases manifesting severe convulsions. It is well-known that violent and protracted muscular contractions produce excessive amounts of sarcolactic acid. Zweifel's demonstration of this acid in the maternal venous and cord blood after eclamptic seizures has already been cited. This and other acid bodies may abstract some of the alkali of the body during excretion and thus cause an acidosis. The fact that an increase in the alkaline reserve of the blood promptly follows the cessation of the convulsions, as in cases 8, 11, and 24, lends support to this explanation. From a surgical standpoint a knowledge of the carbon dioxid combining power of the blood is of prime importance. No patient should be subjected to general anesthesia and operation until the alkali reserve of the blood has been brought up to normal. The manner of doing this has been described under hyperemesis.

The chemical changes noted in the blood in hyperemesis are analogous to those in post-partum eclampsia and eclampsia with gravid uterus. These findings are of interest in view of the statement of Ewing that pernicious vomiting and eclampsia are identical in nature and have the same etiology. In both conditions a general clinical improvement appears to be consequent to a resumption of the normal composition of the blood. In case 11 the toxic symptoms disappeared five days after delivery, and at this time the blood was found to be normal. But it was only after a period of fourteen days that cases 8 and 22 presented evidence of improvement.

Nonprotein Nitrogen Distribution. A study of the nonprotein nitrogen distribution in the fetal circulation and a comparison with that in the maternal circulation has been attempted by numerous workers. Slemons and Morris have determined the nonprotein and urea nitrogen in the cord blood and maternal venous blood at the end of labor. In the maternal blood they obtained an average nonprotein nitrogen of 25.2 milligrams, a urea nitrogen of 10.4 milligrams—44 per cent of the nonprotein nitrogen. In the fetal blood (presumably the umbilical venous blood) the nonprotein nitrogen averaged 24.9 and the urea nitrogen 10.4, or 45 per cent of the nonprotein nitrogen. Slemons and Bogert have made simultaneous determinations of the uric acid in the maternal venous blood and the blood of the umbilical vein. Equivalent values were found for the uric acid in both specimens of blood.

Ploss has come to similar conclusions with regard to the creatinin. Caldwell and Lyle have found the nonprotein and urea nitrogen and creatinin in maternal and fetal blood practically identical in 20 cases at the end of labor. These authors do not state whether the fetal blood was arterial or venous. Obviously from such results no conclusions can be drawn concerning either the functions of the placenta or the origin of toxic factors in the toxemias.

Umbilical Vein and Artery.—Cherry and Killian have succeeded in separating the blood of the umbilical vein from that of the umbilical arteries and a comparison of the nitrogen-partition in these specimens with that in maternal venous blood in normal and toxic cases has brought to light some points of interest. In some cases the nitrogen-partition of the spinal fluid has also been determined.

TABLE IX

A Comparison of the Nonprotein and Urea Nitrogen and Uric Acid of the Maternal Venous and Umbilical Venous and Arterial Blood and of the Maternal Cerebrospinal Fluid

Patient	Blood of	Non-protein N (Mg. per 100 c.c.)	Urea N (Mg. per 100 c.c.)	Urea N Per Cent of Non-protein	Uric Acid (Mg. per 100 c.c.)	Remarks
A. B.	Maternal vein	25	12	48	2.3	Normal
	Umbilical vein	21	11	51	2.8	
	Umbilical artery	33	10	30	4.9	
M. H.	Maternal vein	37	11	29	4.2	Eclampsia
	Umbilical vein	42	13	30	3.8	
	Umbilical artery	53	9	17	7.0	
	Maternal cerebro-spinal fluid	22	10	44	Trace	

The umbilical arteries are carrying blood from the fetus to the placenta, and this blood is actually venous in character. The umbilical vein is transporting the purified or arterial blood from the placenta to the fetus. In the normal case in Table IX the blood of the umbilical vein has approximately the same composition as that of the maternal circulation. In this our findings

are in accord with those of Slemons and Bogert. The blood of the umbilical artery (venous), however, shows a higher nonprotein nitrogen and a greater concentration of uric acid. It also will be noted that the ratio of the urea nitrogen to the nonprotein nitrogen is much less than that of the umbilical venous or maternal blood. In the eclamptic patient also, the maternal and umbilical venous bloods have similar nitrogen-partitions. However, the umbilical arterial blood forms a marked contrast to this. Here there is a marked increase in the nonprotein nitrogen, and a decrease in the urea nitrogen, the urea nitrogen forming only 17 per cent of the nonprotein nitrogen. The uric acid concentration is nearly double that of the umbilical venous blood. It would appear from such results as these that the increase in the nonprotein nitrogen in the maternal blood in eclampsia may be due partly to an absorption of nitrogenous bodies from the fetus.

Cerebrospinal Fluid.—The study of the nitrogen distribution of the cerebrospinal fluid in eclampsia was undertaken to determine whether the pronounced disturbance of the central nervous system are due to a diffusion of the toxic element into the spinal fluid. It will be observed in the case recorded in the table that the nonprotein nitrogen of the cerebrospinal fluid is but 60 per cent of that of the maternal blood, but the urea nitrogen is about 90 per cent. Hence in the spinal fluid the urea nitrogen forms a larger fraction of the nonprotein nitrogen than in the blood. In the cerebrospinal fluid the amount of uric acid was too small to estimate. Myers and Fine report that in 15 miscellaneous cases showing varying degrees of nitrogen retention, the concentration of urea in the spinal fluid averages 88 per cent of that of the blood, and the uric acid but 5 per cent. The authors state that these percentage differences represent the order of solubility of the compounds in water, and apparently also the order of their diffusibility. The concentration of urea nitrogen and of the uric acid in the cerebrospinal fluid in eclampsia is in agreement with the results of Myers and Fine, but there is a marked difference in the relative amounts of nonprotein nitrogen. This fact would lead us to believe that some of the components of the increased nonprotein nitrogen of the eclamptic blood are less diffusible than uric acid, and that the disturbances of the central nervous system in this toxemia cannot be due to the diffusion of the toxic element into the cerebrospinal fluid.

Chart I (Fig. 1) presents graphically the average values for nonprotein and urea nitrogen and uric acid in cases of normal pregnancy, chronic nephritis, nephritic toxemias, hyperemesis and eclampsia. It is evident that in nephritic toxemias the relation of the urea nitrogen to the nonprotein is analogous to that characteristic of chronic nephritis. But in hyperemesis and eclampsia the disturbance of this relation is very striking. It will also be noted that the average value for uric acid in the eclampsias is greater than in chronic nephritis or the nephritic toxemias.

SUMMARY

Low values for nonprotein and urea nitrogen are found in normal pregnancy. The urea nitrogen constitutes about 44 per cent of the nonprotein nitrogen. No variation is found in the uric acid, creatinin, chlorid or sugar concentration of the blood of normal pregnant women from that observed in nonpregnant women. A slight decrease in the carbon dioxid combining power of the blood plasma characterizes the last months of normal pregnancy.

The chemical changes in the blood in the nephritic toxemias are typical of impairment of kidney function in general. There is an increase in the nonprotein and urea nitrogen, and more than 50 per cent of the nonprotein nitrogen is in the form of urea. There is a decrease in the alkali reserve of the blood, but no greater than that observed in normal pregnancy.

Analogous chemical changes are found in the blood in hyperemesis, post-partum eclampsia and eclampsia with gravid uterus. The nonprotein nitrogen is markedly increased whereas the urea nitrogen is at the low normal limit or decreased, constituting but 15 to 38 per cent of the nonprotein nitrogen. A definite increase in uric acid is found which is due to an impairment of renal function. In some cases the disturbance of kidney function resulted in a retention of urea nitrogen in addition to the uric acid. In these types of toxemia, the involvement of renal function results from the toxemia. A moderate or severe acidosis is observed in all cases. A prompt improvement judged from a clinical standpoint is accompanied by a return to a normal composition of the blood. The extent of the toxemia closely parallels the increase in the

rest-nitrogen, as judged by the relation of the urea to the non-protein nitrogen.

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ILLUSTRATIVE CASE REPORTS

The brief descriptions which follow are taken from personal case records and, while very much condensed, will, it is hoped, demonstrate typical instances of some of the many variations of the toxemias of pregnancy.

The patients were seen in the service of the New York Lying-in Hospital or in the author's private practice, unless otherwise noted.

Dates, hospital numbers and other designations are purposely omitted as unnecessary.

1. *Severe Hyperemesis in First Pregnancy with Complete Absence of this Complication in Subsequent Pregnancies.*—The patient, in good general health, a para-i, began to vomit soon after skipping a period and notwithstanding treatment her condition grew rapidly worse. From being a well-nourished girl with florid complexion, she lost weight rapidly and developed a marked pallor of the skin which later became yellow and the conjunctivæ were markedly injected. The patient was very anxious to carry out her pregnancy, but when she began to vomit large quantities of coffee-ground material, it was decided to empty the uterus. This was done in two sessions without shock and the patient made a fairly rapid recovery. Subsequently she went through two full-term pregnancies without any vomiting at all. In each case the labor was rather difficult. In her fourth pregnancy she began to vomit within a short time after the missed period. Her general condition was fairly good, but she was very nervous and depressed. She began to bleed and finally passed several large clots. A diagnosis of incomplete abortion was made, and an exploratory curettage was done. A moderate amount of detritus was secured but no placenta was found. Evidently the abortion had been fairly complete. Unfortunately, the softened cervix was torn during the process of dilatation and the patient's subsequent recovery was marked by moderate elevations of temperature

with the production of a pelvic exudate. The final recovery was fairly good, however. Why this severe hyperemesis should have been present only in the first and not in subsequent pregnancies, could not be determined. There were evident local causes. It is interesting to note that with the reappearance of the trouble in the fourth gestation, spontaneous abortion resulted.

2. *Induction of Labor for Death of Fetus and Toxemia.*—Patient age twenty-four, married two years, had a spontaneous miscarriage at the end of her first year at two months, following what was diagnosed at the time as a "renal infection." In her second pregnancy there were traces of albumin from the beginning, although her general health was apparently good. When I saw her at the sixth month the urine showed about 2 per cent albumin, but no casts. The blood-pressure was 160 over 110. An effort was made to carry the patient along, as she was very anxious for a child. She was kept in bed on a restricted diet and after an apparent improvement she was allowed to go home. Two weeks later the baby could no longer be felt and during the succeeding two weeks no further enlargement of the uterus seemed to take place. As the patient was very thin, with relaxed abdomen, this could be readily noted. Careful examination showed no evidences of fetal movements or heart signs. The patient's general condition was not good. She complained of headaches, nausea and vomiting. The face was puffy and there was slight edema of the hands and feet. The albuminuria increased and, in the belief that the toxic symptoms were due to a combination of the nephritis and a dead fetus, labor was induced with bags and after sufficient dilatation a breech extraction of a macerated six months' fetus was performed. The placenta was found to be thickly studded with infarcts, one of which measured about two inches in diameter. It is likely that in this case the fetal death could be ascribed to the placental degeneration induced by the nephritis in the mother. A year later the patient again became pregnant. During the interval she had been in fairly good general condition, having gained in weight since her previous pregnancy, but as soon as she became pregnant again her condition immediately grew worse. Nausea and vomiting were extreme. Headaches and visual disturbances were constantly present and her weight diminished. The examination of the urine at this time showed increasing amounts of albumin and numerous casts, a

progressive condition which it was not thought the patient could satisfactorily overcome. The uterus was accordingly emptied and the patient made a fairly prompt recovery. She was warned not to become pregnant for several years and to place herself under competent observation at the very beginning of her pregnancy.

The patient remained in good general health, gained weight and became pregnant again about two years later. Aside from mild nausea and vomiting she remained apparently well until the sixth month of her pregnancy, when the urine, which had contained only slight traces of albumin, suddenly contained from two to four grams per liter and numerous hyalin and epithelial casts appeared. Under the care of her family physician, her condition improved but about three weeks later she noticed a numbness in the right arm which gradually extended upward and developed into a more or less complete paralysis of the entire limb and the pectoral group of muscles. Loss of speech followed, with a paralysis involving the tongue and right side of the face. There was no period of unconsciousness. The patient responded to questions by attempting to nod her head. Both pupils reacted equally to light, the tongue could be fully protruded but the tip deviated to the left. There was no loss of tactile sense except in the right arm from the finger tips to the shoulder. The limb was warm to the touch. Swallowing was somewhat interfered with although the patient was able to take liquids slowly. The uterus was apparently that of 6½ to 7 months' gestation and the fetal sounds were faintly heard over the lower uterine segment. Fetal movements were distinctly felt by patient. Blood pressure 160 systolic, 90 diastolic. The condition impressed one as due to localized cerebral edema rather than actual hemorrhage. Patient transferred to the hospital and on admission the urine showed 10 grams per liter with numerous hyalin and granular casts; there was no acetone or diacetic acid present.

Treatment by hot packs and colonic irrigations with glucose solution, together with forced carbohydrate feeding and sedatives by rectum was succeeded by a gradual improvement in the patient's condition until all evidences of paralysis disappeared one month after admission to the hospital.

The abdominal enlargement did not seem to progress and, although the patient believed she was over seven months' pregnant, the fundus corresponded in size to less than this period.

Fetal movements were distinctly felt and heart sounds heard during this time and then ceased suddenly. After several days of observation it was thought advisable to induce labor and this was completed without difficulty, a poorly nourished infant of about seven months' gestation being born. No abnormalities were present except that the cord was around the neck in a loose coil not sufficiently tight to have produced constriction. There was a slight degree of maceration of the epithelium around the feet. The placenta was easily expressed and there was no retroplacental clot; post-partum hemorrhage was slight. The placental substance was thin and contained numerous infarcts, making up about one-half of its mass, quite typical of this condition.

The patient made an uninterrupted recovery and was discharged from the hospital two weeks later with a normal urinary picture. In this instance it is very unlikely that the patient will ever carry out a full-time gestation.

3. *Induction of Labor for Mild Toxemia.*—Patient, a para-i, age thirty-five, in fairly good general health, presented nothing abnormal until the seventh month, when she developed some dyspnea, had repeated slight fainting spells and became very nervous. The blood-pressure up to the eighth month had been practically normal, but gradually increased until the systolic pressure was 172 at the calculated termination of her pregnancy. There were no evidences of labor present and no response to several doses of castor oil. Considerable malaise and a decided yellow tinge to the skin and sclera became prominent symptoms and, although the urine examinations were negative, the picture was one of a gradually increasing toxemia. Labor was induced with bags and proceeded slowly, a forceps extraction being done when the head reached the perineum. The baby was large and vigorous. The patient made a slow recovery, although the involution of the uterus proceeded normally. Several months later a diagnosis of hypothyroidism was made and considerable improvement resulted from specific treatment for this condition.

The case is one of a considerable group met with in which the endocrine disturbances centered in thyroid anomalies seem to be prominent. Their treatment during pregnancy is very unsatisfactory and little improvement occurs until after delivery. Strange to say, in many of these patients the babies are large and well-nourished, which adds considerably to the difficulty of the

labor. The patients present evidences of toxemia which, although mild in degree, are continuous and always require careful observation of the patient, with a resort to more vigorous treatment when indicated, including the induction of labor if the patient does not spontaneously go into labor at term.

4. *Induction of Labor for Nephritic Type of Toxemia.*—The patient, a young primipara at the seventh month, had been under continuous treatment for the previous two months. The blood-pressure at the beginning was about 180 and accompanied by puffiness of the face and a persistent albuminuria (from 4 to 6 per cent). A few granular casts were noted occasionally. There were slight visual disturbances and considerable headache. At the eighth month the patient's condition did not improve and induction of labor was decided on. This was successfully started with bags, but the patient made slow progress and was finally delivered by low forceps. The baby was considerably asphyxiated, but was finally resuscitated and, although weighing less than five pounds, did very well on artificial feeding.

The patient made a slow recovery, and the albumin persisted for some months after delivery, although the edema disappeared more promptly. Labor was induced in this instance a month before term because it was felt that the progressive character of the nephritis might produce irremedial damage if the patient were allowed to go for an indefinite period.

5. *Eclampsia During Midpregnancy in a Patient with Chronic Nephritis; Exacerbation in Second Pregnancy with Induction of Labor and Delivery of a Viable Child.*—The patient, a primipara, was seen in consultation when about six months' pregnant, with a history of having had three general convulsions, after the first of which she had been transferred to a hospital. Examination showed a stout, well-nourished girl in deep coma, with marked puffiness of hands, face and feet. The abdominal fat was thick and the fundus slightly above the level of the umbilicus. There were no evidences of labor. Previous urinalyses showed increasing traces of albumin, but no definite treatment had been instituted. The patient's general condition seemed unfavorable for any attempts at palliative treatment, so induction of labor was carried out by means of Voorhees bags without difficulty. The convulsions continued during the labor, and, after sufficient dilatation was secured, the membranes were ruptured and the fetus ex-

tracted with the hand. It weighed about one pound, was about nine inches long and made no efforts at respiration. The patient made a very slow recovery and the albumin and casts persisted in the urine for many weeks. She became pregnant again about four years later and was seen in consultation at the sixth month. Her physician had carefully watched the case and at this time, although there was some general edema, the blood-pressure was fairly low and the urine did not contain any casts, although a moderate amount of albumin was present. In view of the desire for a living child an attempt was made to carry the patient along. Hospital sojourn was instituted and the patient kept in bed on a carefully regulated low protein diet. The edema and slight headaches persisted, but the blood-pressure did not go over 150 and only slight traces of albumin with few casts were noted in the urine. About the eighth month the patient complained of dizziness and one evening noticed slight twitching movements of the hands and face. The general condition was not as favorable as during the previous weeks, and labor was accordingly induced with Voorhees bags. Within twenty-four hours the patient delivered herself of a small but vigorous baby, which, after a preliminary bottle period, was successfully nursed. The patient made a very satisfactory recovery from this labor and, although subsequent urinalyses showed that her nephritis was not recovered from, her general condition seemed very satisfactory. The case demonstrated the possibility of carrying these patients through a subsequent pregnancy notwithstanding an unfortunate previous attempt.

6. *Induction of Labor for Toxemia and Thyroid Disturbances.*—Patient, a para-i of neurotic temperament, went through a very uncomfortable pregnancy marked by headaches beginning during the early months, to which, after the sixth month, were added visual disturbances and swelling of the hands and feet. There were marked traces of albumin in a urine of high specific gravity. When the patient was about eight months' pregnant the condition of hydramnios and edema of the lower part of the abdomen made her very uncomfortable. The patient had an exophthalmic goiter; by advice of another physician thyroid extract was administered continuously at this time. Her general condition, with high blood-pressure and unfavorable urinary signs, called for interference, and labor was induced with Voorhees bags. The response

was unsatisfactory, the patient's condition becoming rapidly worse. Rupture of the membranes was performed when the cervix was about three fingers dilated to relieve the extreme abdominal tension and also in the hope that the head might engage. No progress resulted for the next twenty-four hours and, as the patient was quite exhausted, no engagement of the head present, the cesarean section was finally decided on notwithstanding the vaginal manipulations. It was a last resort operation and performed without much difficulty. The baby was deeply asphyxiated at the time of extraction and resuscitation was unsuccessful. This failure could be attributed to the intense uterine contractions produced by pituitrin which, contrary to directions, had been given too early in the procedure. Notwithstanding the unsatisfactory outlook, the patient made a fairly good and rapid recovery from her operation. The evidences of nephritis persisted for several months and the condition of asthenia did not respond well to tonic treatment. The exophthalmus and thyroid enlargement was very much worse six months after delivery when the patient disappeared from observation.

7. *Induction of Labor for Hydramnios with Mild Toxemia and Thyroid Disturbance.*—Mrs. P., at or near term in her second pregnancy, presented an extreme degree of abdominal distention which had been progressing for the previous two months. During this period she had repeated attacks of severe headache and dizziness, combined with nausea and general malaise, together with a moderate swelling of the hands and feet. The right lobe of the thyroid became considerably enlarged during this time and, although the termination of the patient's pregnancy was not calculated until a month later, it was not considered advisable to allow her to continue because of the increasing distress. The urine at this time showed moderate traces of albumin and the blood-pressure was moderately high. Labor was started with a No. 3 Voorhees bag and completed within twenty-four hours. Rupture of the membranes after complete dilatation permitted the escape of a gallon or more of liquor amnii after which the labor was promptly terminated. The baby was large and well-nourished and the placenta normal. The symptoms promptly disappeared within a week after delivery, but the thyroid enlargement progressed and about a year later a partial thyroidectomy was performed with good results. During this patient's first

pregnancy a much less degree of thyroid enlargement was present, but there were no evidences of toxemia like those that became prominent after the seventh month of her second gestation.

8. *Doubtful Eclampsia with a Single Convulsion.*—Mrs. ——, a primipara, was admitted to the hospital with a history of having been perfectly well until she went into labor when, during the active first stage, a single general convulsive seizure occurred. The patient was rushed to the hospital and was given eliminatory and sedative treatment. She had a spontaneous delivery within a few hours. There were no further convulsions and examination of the urine showed only a faint trace of albumin and no casts. There was no elevation of blood-pressure. It is doubtful whether this case can be considered a true eclampsia, or may be regarded purely as an explosion of nervous force during the active first stage of labor, similar to what we see in young children who often develop a convulsion during the process of teething or otherwise.

9. *Pre-eclamptic Toxemia with Induction of Labor, Cervical Incision and Forceps Delivery.*—The patient, a para-i, was admitted to the hospital during the seventh month of her pregnancy with a well-developed nephritis. She was kept under observation for two weeks, but very little improvement followed the usual dietary and eliminant measures. Marked puffiness of the face and hands continued; the urine contained well-defined traces of albumin and many hyaline and granular casts. Examination of the eye-grounds showed considerable edema of the retina but no hemorrhages and the ophthalmologist called in consultation believed that the case should be delivered. The induction of labor was started with a rectal bougie and vaginal pack. The cervix was rigid, scarcely dilated, but on removal of the bougie after twenty-four hours, the cervix was found to be soft, dilated one finger breadth and thinned out. A No. 2 Voorhees bag was next introduced which brought on regular pains and was expelled about twenty-four hours later. The cervix was then only two fingers dilated and rigid. The fetal heart became more rapid and during the afternoon the rate went up to 170. The patient complained bitterly of headache and visual disturbances. In view of the patient's condition and also that of the child, rapid delivery was decided on, and under light anesthesia the anterior lip of the cervix was incised to the vaginal vault. A sufficient opening was

secured to deliver the small head with forceps. The baby was markedly asphyxiated and was resuscitated with difficulty. It was small and poorly nourished and died subsequently from inanition. The placenta was the site of many infarcts and areas of fatty degeneration. The cervical incision was immediately closed and was satisfactorily healed at the time of discharge. The woman recovered quickly after delivery and, in view of the small and poorly-nourished child, more time could have been allowed for the dilatation of the cervix rather than a resort to a cutting operation. The latter was inspired as much by the mother's condition as by a desire to save the child, as a convulsive seizure seemed imminent. The eye lesions subsided rapidly after delivery.

10, 11. *Confusion of Eclampsia with Encephalitis Lethargica.*— The patient, a para-i, was admitted to hospital with a history of having suddenly developed convulsions at the seventh month, which were followed by coma. The urinary examination seemed to point to a moderate degree of toxemia and after twenty-four hours the patient recovered from her coma. The blood-pressure was not high and a temperature of about 102° F., was constant. Within twenty-four hours she developed further convulsions, succeeded by coma with motor and sensory disturbances of the extremities and rigidity of the neck. A diagnosis of either cerebral hemorrhage or meningitis was made and a lumbar puncture was performed. The fluid showed the typical characteristics of the encephalitis epidemic of which many cases had been reported at that time in New York City. The condition grew rapidly worse with deepening coma, increasing temperature, delirium, and finally death within about three days after admission to the hospital. The diagnosis of encephalitis was confirmed by the consulting neurologist and the case shows the necessity of care in instituting treatment in such cases. The fetal heart was not heard at any time and the patient died undelivered, not being considered at any time in a condition for operative interference.

In another case admitted to the hospital at the same time with a similar history, the subsequent course was very much milder and, the diagnosis having been made, the patient was transferred to Bellevue Hospital. She was at about the seventh month of pregnancy and made a complete recovery and was readmitted at term to the Lying-in Hospital, where she delivered herself spontaneously of a live baby and made an uneventful recovery. In

this case also the general impression, even before the neurological diagnosis was made, was that the case was not a toxemia of the type ordinarily met with in pregnancy.

12. *Cardiac Disease Associated with Toxemia at the Seventh Month.*—Mrs. ——, para-i, was admitted to the hospital with a history of dyspnea on exertion which came on rather suddenly two weeks previously. The patient, a stout, well-nourished woman with florid complexion, was at about the seventh month of pregnancy. No fetal heart was heard or evidence of life elicited. The urine contained a marked trace of albumin with no casts except on one occasion. The blood-pressure was about 160. The patient was markedly dyspneic on admission and the mucous membranes cyanotic. Examination of the heart showed a double mitral murmur with marked galloping rhythm. A well-defined area on the anterior left chest presented numerous coarse râles and what appeared to be friction sounds over the cardiac area itself. The apex beat was moderately displaced. A diagnosis was made of endocarditis complicating the pregnancy with partially broken compensation at the time she began to have dyspnea two weeks previously. The high blood-pressure and urinary signs pointed to an associated toxemia, but the serious symptoms could be ascribed to the former, rather than to the latter, lesion. With rest in bed the signs in the lungs and heart rapidly disappeared so that it was difficult to detect any murmur three days later when the patient went into labor spontaneously and delivered herself of a small, poorly-nourished, macerated fetus of about seven months' gestation. Examination of the placenta in this case showed a slight degree of fatty degeneration but no other visible abnormality. The patient improved rapidly after delivery, and the urinary signs disappeared within three days, although the dyspnea persisted. This case, as others, shows the necessity of making a careful physical examination in every suspected eclamptic.

13. *Pre-eclamptic Toxemia, with Cesarean Section.*—The patient was admitted to hospital for observation, complaining of headaches and marked visual disturbances. She was a para-i, about thirty-five years of age and apparently about seven and one-half months' pregnant. She was a well-nourished woman inclined to stoutness, with marked edema of the legs and puffiness of face and hands. Under the usual eliminant treatment with irrigations and

hot packs, together with a diet restricted largely to carbohydrates, a rapid diminution in the urinary albumin occurred, and also in the number of casts. The patient was carried along for over three weeks and then began to get worse again, complaining of severe headaches and visual disturbances, including transitory periods of actual blindness. The urine then boiled solid and in view of the rapid onset of the symptoms, cesarean section was decided on, as the cervix was elongated and undilated. The cesarean operation was performed according to the Davis procedure and both mother and baby did very well. On the tenth day post partum the patient had a severe coughing spell and ruptured the uterine wound with protrusion of the intestines. An immediate closure was done by my associate, Dr. L. A. Wing, who stated that the edges of the wound were perfectly clean. The second repair resulted in a firm, satisfactory closure. During no time did the patient have any temperature, and she left the hospital in good condition and nursing her baby. Failure in the union in the abdominal wound has been noted in other cases of toxemia delivered by cesarean section, where no evidences of infection can be found.

14. *Fulminating Eclampsia with Recovery and Subsequent Death from Cerebral Hemorrhage.*—A primipara at about the seventh month of pregnancy was admitted to the hospital with a history of sudden onset of general convulsions. There was no record of previous ante-partum care. The patient was a small, well-nourished woman in coma, with moderate swelling of hands, feet and ankles. The fundus was about seven months' and the fetal heart sounds were not heard. The patient had several convulsive seizures during the next two days. Repeated doses of morphin by hypodermic seemed to exert very little sedative effect, and it was not until the rectal administration of 40 grains of chloral and 60 grains of sodium bromid that the patient quieted down. She was so restless that it was impossible to administer either hot packs or irrigations. After quieting down as the result of the rectal administration, packs and irrigations were given twice daily, and within twenty-four hours she began to come out of coma and in a few days seemed completely recovered.

The urine was solid on admission and for several days subsequently and then quickly cleared up. One week later the patient insisted upon going home and became very much excited because

of the noise from the adjacent delivery room. That evening she again began to have general convulsions; the urine boiled solid and no response to treatment was obtained. About twenty-four hours after the beginning of the second seizure she developed Cheyne-Stokes respirations and died in coma without further convulsions about six hours later. No autopsy was permitted in this case. The picture was that of a cerebral hemorrhage, probably into one of the ventricles or at the base of the brain. Spontaneous delivery of a small, living baby took place during the second attack, the patient apparently being unaware of labor. The baby weighed 1,600 grams and lived about a week.

15. *Induction of Labor for Recurrent Albuminuria.*—The patient was feeling well but was admitted to hospital for observation because a routine urine examination showed solid albumin with many hyaline and granular casts. No general symptoms were present. The patient was given a light carbohydrate diet and the bowels were thoroughly cleared out with castor oil and enemas. The urinary conditions improved and for several days there was merely a trace of albumin, but a sudden recurrence marked by solid albumin and a complaint of malaise, headache and dizziness prompted the induction of labor. A soft rubber rectal tube was inserted through the rather thick cervix, which admitted one finger, and within twenty-four hours the patient delivered herself spontaneously of a vigorous baby. Within a few days the urine cleared and the patient left the hospital on the tenth day with no albumin or casts.

In this woman, a multipara, evidently near term, there seemed to be no reason for delaying the delivery in view of the warning given by the recurrence of the albuminuria and the development of constitutional symptoms.

16. *Induction of Labor for Progressive Toxemia.*—The patient, a para-iv, age thirty-five, with a history of profuse menstruation and a toxemia in previous pregnancies, developed a moderate toxemia about the sixth month. The patient was stout, apparently well nourished, and with regular heart action. The blood-pressure was 164/108, and a slight systolic murmur was present. After a week's treatment, including colonic irrigations, diet and rest in bed, a marked improvement resulted and the patient was dismissed from the hospital. At the end of June, when she was at about the eighth month, a marked swelling of the legs and lower

abdominal wall came on, with headache and a systolic blood-pressure of 180. During this time the urine contained traces of albumin and no acidosis, but the blood showed a high sugar content. In view of the general discomfort and apprehension, labor was induced with bags and terminated by an easy low forceps delivery. The baby weighed nine pounds. The placenta was very thick, showed several areas of fatty degeneration and two cysts of about an inch in diameter near the insertion of the cord. The outcome might have been less favorable in this case, especially for the child, if the pregnancy had continued. Stout women of this type developing toxemia are not good risks.

17. *Toxemia at the Seventh Month with Premature Separation of Placenta at Term.*—A private patient, age thirty, otherwise well, but stated that she had gained over twenty pounds since her marriage a year previously. The woman was very stout and the early diagnosis of pregnancy difficult. An adnexal tumor or fibroid was suspected as present and complicating pregnancy. The patient went along under careful observation until September, 1921. At this time she began to complain of drowsiness and marked tingling sensations and swelling of the hands which kept her awake at night. Careful urine examinations showed a low specific gravity, slight traces of albumin with a low urea output, but no casts. A moderate degree of anemia was present such as one might expect in a pale, flabby patient of this type. The blood-pressure at no time was over 140, but a moderate edema of the legs developed. Not responding to the usual measures, the patient was sent to the hospital and within a week after beginning radical eliminant treatment with colonic irrigations and hot packs, the symptoms rapidly subsided and after dismissal the patient complained only of slight tingling sensations in the hands. A moderate dyspnea was present throughout the later months. The patient's labor was calculated for October 30, but at this time there were no evidences of its appearance and, as her general condition was good, it was decided to await a natural termination of the pregnancy. On November 15, 1921, the patient was given two ounces of castor oil with good result, and no pains were observed. While playing cards on the evening of the following day a sudden hemorrhage occurred without pain. Examination about an hour later showed that the patient had bled pretty freely. The vagina was full of clots; the cervix long, rigid, high,

slightly dilated but no presenting part was felt. The pulse was good, though somewhat rapid. The patient stated that she had not felt any life since six o'clock in the evening. A tentative diagnosis of premature separation of the placenta was made, with fetal death. The patient was transferred to the Women's Hospital and immediate preparations were made for cesarean section. Approach was made through the median high incision, and no blood was found in the free peritoneal cavity. On incising the uterus a considerable part of the placenta, which was evidently free from the uterine wall, protruded into the wound and the placenta itself was attached along the right side of the uterus, extending down to the lower segment. On rupturing the amniotic sac it was found filled with blood and the child when extracted appeared completely exsanguinated. The uterus contracted well after the removal of the placenta and was the site of at least a dozen fibroid nodules. One as large as a pigeon's egg in the anterior wall appeared to be breaking down and it was therefore clamped and excised. The fetus was not well nourished and was completely exsanguinated. A cause for the latter was found in the velamentous insertion of the cord into the upper portion of the placenta and apparent rupture, allowing the fetal hemorrhage to take place. An examination of the placenta showed a separation of several finger breadths and numerous infarcts. The patient made an uninterrupted recovery. The wound healed by primary union, there was no shock, and the urinary conditions were practically negative throughout the puerperium.

In this patient we were evidently dealing with a moderate degree of toxemia which produced alterations in the placenta that interfered decidedly with the nutrition of the fetus. The velamentous insertion of the cord had no connection with the toxemia and it is doubtful whether enough placental separation had occurred to kill the baby had it not been for the rupture of the cord. It might be surmised that this thinned-out insertion was torn during the extraction, but the distinct statement by the patient that she no longer felt life before the hemorrhage took place and the fact that no heart sounds could be heard pointed to the death of the fetus from hemorrhage.

18. *Marked Toxemia in Middle Months of Pregnancy.*—The patient, age twenty, para-i, about five months' pregnant, was admitted to the hospital with a history of gradually increasing

edema during the previous weeks, involving, in succession, the lower extremities, hands, face and labia. The latter were enlarged to such an extent that micturition was difficult. Examination of the urine showed marked traces of albumin, a moderately high specific gravity and many hyaline and granular casts. The patient was under observation for a week under eliminant treatment without amelioration of symptoms. Headaches became more marked and the blood-pressure averaged 160 systolic. In view of the youth of the patient and the early appearance of the marked nephritic symptoms, emptying of the uterus was decided upon as giving the patient a better chance for a future pregnancy before serious damage to kidneys took place. Vaginal hysterotomy was followed by prompt cessation of the symptoms, lowered blood-pressure and disappearance of the edema.

19. *Spontaneous Abortion during Toxemia.*—The patient, a para-iv, age thirty-four years, with a history of three previous normal labors and living children. In the fifth month of her present pregnancy she developed severe headaches, epigastric pain and a variety of nervous symptoms. The patient was apparently neurotic, although she appeared well nourished. On her admission to the hospital, examination disclosed a pregnancy at about the fifth month, with a history of slight bleeding. The blood-pressure, which was 180 on admission, diminished with rest in bed during the succeeding week, but remained about 150. The patient went into labor spontaneously and delivered herself of a small, macerated fetus. The urine showed marked traces of albumin and contained many hyaline and granular casts. The termination of pregnancy in toxemias during the midmonths is not unusual and, as in this case, proves a satisfactory conclusion to the process.

20. *Cesarean Section for Eclampsia in First Pregnancy; Second Pregnancy and Labor Normal.*—The patient, a para-ii, was admitted to the hospital at eight and one-half months with a history of a previous cesarean section for the termination of her first pregnancy, with living child. There was no evidence of toxemia during the present pregnancy. The patient was kept in bed under careful observation and went into labor spontaneously, apparently at term. The membranes were ruptured when the cervix was two fingers' dilated in order to relieve the tension on the uterine wall. Dilatation proceeded rapidly, the head came down to the level of the spines and the delivery of a normal living child was

completed by forceps. In this instance the cesarean section was done by another operator for the relief of severe convulsions, evidently with a satisfactory outcome. The nonappearance of evidences of toxemia in her second pregnancy may perhaps be attributed to the careful ante-partum observation. The case also shows the advisability of keeping these patients in the hospital under observation during the last weeks of subsequent pregnancies and the fallacy of reliance on the dictum: "Once a cesarean, always a cesarean."

21. *Convulsions Due to Cerebral Abscess During Pregnancy Which Closely Simulated Eclampsia.*—This complication was well demonstrated in a case reported by Coughlin in the *Long Island Medical Journal,* March, 1921. The patient, a para-i, age twenty-four, suddenly developed general convulsions and was admitted to the hospital as an eclamptic and was treated accordingly. A macerated fetus was spontaneously expelled, and, after labor, the patient went into a condition of coma. Within a few days meningeal symptoms became marked and the patient died. The autopsy showed a cerebral abscess and the infective organism was a diplococcus intracellularis. It is possible that in this case a condition of sepsis may have developed after delivery, as we know eclamptic patients are particularly prone to sepsis, but in all probability the cerebral lesion antedated the labor.

22. *Fatal Case of Hepatic Type of Eclampsia.*—The patient, a para-i, age nineteen, was admitted to the hospital in a condition of coma which followed a spontaneous labor with forceps delivery on the previous day. The patient had apparently been well throughout her pregnancy until she was suddenly seized with convulsions, of which there were a total of twenty-one before she became comatose. A diffused, deep jaundice developed. The woman did not again become conscious and died after having had one more convulsion about forty-eight hours after delivery. An autopsy showed a large liver weighing about 2,500 grams and presenting numerous subcapsular hemorrhages scattered over its entire surface (see Fig. 16), and in addition, there were many hemorrhagic areas on section of the organ. A microscopical examination showed necrosis, autolysis and disintegration of the hepatic cells of the central two-thirds of the liver lobule. There were also many larger hemorrhagic areas throughout the liver substance which destroyed the hepatic cells from pressure. There was only a small amount of fatty degenera-

tion present, although many of the cells showed a cloudy swelling. The kidneys were the site of an acute diffuse nephritis. A few petechial hemorrhages were noted in the spleen. The lungs were edematous and many of the air cells filled with blood. This was one of those fulminating cases in which the sudden and severe onset precluded a satisfactory prognosis notwithstanding the early delivery of the patient.

23. *Induction of Abortion for Toxemia in the Middle Months of Pregnancy.*—The patient, a para-iv, age twenty-two, had had one stillborn child at the eighth month as the result of eclampsia and another five months' miscarriage. The woman, although stout and apparently well nourished, was of a very nervous temperament with many complaints, including insomnia, restlessness, headaches, etc. Very little coöperation was secured from the patient in an attempt to alleviate her condition. The headaches grew steadily worse and were accompanied by visual disturbances which came on in attacks of which several were characterized by periods of complete blindness. The examination of the eye-ground was not satisfactory. There was no edema at any time and the blood-pressure remained within normal limits. The patient finally went into labor and delivered herself spontaneously of a full-term apparently healthy baby. About two years later she again became pregnant and, when she reached her fourth month, the evidences of toxemia again became marked. The visual disturbances and dizziness were accompanied by moderate traces of albumin in the urine and many hyaline and granular casts. She developed a considerable edema of the legs and hands and her general nervous condition made one very apprehensive as to the final outcome. After due consultation it was decided to empty the uterus and this was done after two cervical packings with gauze and a small Voorhees bag. After sufficient dilatation was secured the membranes were ruptured and the fetus extracted by the feet. The fetus had apparently been dead for some time, as the head came away during the process of extraction. A spina bifida was also present in the sacral region.

This patient had, after getting up, several subjunctival hemorrhages and since then has occasionally been troubled with an exacerbation of the nephritis, including attacks of headaches, dizziness, swelling of the feet, etc. This woman has been warned against any further pregnancies.

24. *Eclamptic Patient Delivered by Vaginal Cesarean Section.*—The patient, a young primipara about eight months' pregnant, was well during the entire pregnancy until a few days previous to admission to the hospital, when she complained of headaches and dizziness. Several convulsive seizures came on without warning and on admission the patient was in a comatose condition. There were no signs of beginning labor. The cervix was long, rigid and thick. Additional convulsions occurred and there was no response to sedatives. At that time I was less inclined to conservative measures than at present and the patient was prepared for delivery by a vaginal cesarean section. The bladder was stripped back after making an incision in the anterior vaginal fornix and then the anterior lip of the cervix was cut in the midline down to the level of the internal os. A combined version was performed without difficulty and a small, feeble child extracted which died a few days later. The uterus contracted firmly and there was little hemorrhage. There was no difficulty in this instance in gaining sufficient opening in the lower uterine segment to do a version with breech extraction, but in attempting to close the operative wound considerable difficulty was encountered, as the upper portion could not readily be approached for suturing; in fact, this took longer than the delivery. Although I had done a series of vaginal cesarean sections on similar indications, I became impressed with my experience sufficiently to give up this operation in such cases, on account of the difficulties of suturing and the loss of time. The abdominal cesarean section was considered in this case, but on account of the number of vaginal examinations previously made, it was not thought safe. The patient finally made a satisfactory recovery.

25. *Induction of Labor for Chronic Nephritis with Visual Complications.*—The patient was about eight months pregnant when admitted to the Misericordia Hospital with a history of increasing visual disturbances during the past two months. Examination by a prominent ophthalmologist disclosed a retinal edema, with impending hemorrhages and induction of labor was advised. The patient, however, was carried along until approximately the eighth month, when labor was induced without difficulty, with a Voorhees bag. Delivery was completed with a low forceps extraction. A small, poorly-nourished baby was born, which weighed three and one-half pounds and died from inanition the

day after delivery. The placenta did not show any gross abnormalities aside from its thin, flattened-out character. The baby presented the typical appearance of one born of a nephritic mother and, although probably somewhat premature, was undoubtedly unfavorably affected by the toxemia of the mother. The patient made a slow but satisfactory recovery. The albumin, casts and edema persisted for some months, and in view of the patient's history and the severe character of her previous pregnancies, a sterilization by the abdominal route was undertaken about a year later when the patient presented herself again at about the second month of pregnancy. The uterus was first emptied through a transverse fundal incision. A good recovery resulted. The patient in this last pregnancy, although only a few months advanced, began to show marked traces of albumin in the urine, together with many casts, and serious eye symptoms also appeared as in the previous pregnancies. In view of these facts it was not thought advisable to allow her to continue or to be subjected again to impregnation.

26. *Fatal Case of Eclampsia of the Nephritic Type.*—A para-ii, about eight months' pregnant, was seized with severe vomiting attacks accompanied by headache. On the same day several convulsions came on, and, on admission to the hospital, the patient was in moderate coma. The pulse was weak and of low tension. The fetal heart could not be heard. The cervix was soft, two fingers' dilated, and the head in the brim. Colonic irrigations resulted in the passage of a large amount of very foul fecal matter. The urine specimen boiled solid. Spontaneous delivery of a normal stillborn, full-term fetus followed. A few slight convulsions were noted after delivery, but the coma was continuous. There was a little improvement on the next day and the patient apparently reacted well to the treatment, but within twenty-four hours after delivery the temperature began to go up and the coma returned. Several severe convulsions occurred throughout the night. The temperature rose to 106° F., the pulse tension increased, and the respirations became shallow, but the color remained good and there was no jaundice. A venesection, followed by the instillation of 1,500 cubic centimeters of normal salt solution, was without result. The convulsions continued and the patient died the next day. A study of this case seemed to point to an overwhelming toxemia with a probable basilar hemorrhage or general cerebral edema coming

on after the period of improvement on the day of labor. Inquiry disclosed the fact that the patient suffered from extreme constipation throughout her pregnancy, and, although she did not feel well before the final fatal attack, no urine examinations were made and nothing further done until the convulsions developed.

I would have considered salt solution contra-indicated if this case had come under my care during recent years, since I have adopted glucose solutions for this purpose.

27. *Eclampsia with Induction of Labor, Version, and Death of Patient.*—The patient, a para-vi, about seven months' pregnant, had been showing considerable albumin and casts in the urine for which treatment had been given with apparently little result. She complained of severe headaches and indigestion and when seen in consultation had had a general convulsion followed by coma. Two further convulsions occurred before the patient could be sent to the Woman's Hospital. The systolic blood-pressure was 152, the respirations about 15 per minute, and the pulse good and full. The cervix was one finger dilated, the vertex presenting, and the fetal heart heard. Against my better judgment I was prevailed upon to proceed with the induction of labor. This was carried out with a Voorhees bag. The dilatation was fairly prompt and within a few hours the cervix was thinned out and four fingers' dilated. The patient's general condition during this time became worse, the respirations being more superficial and the pulse rapid. Although there were no further convulsive seizures, irregular twitching movements of the hands were noted. Moderately strong uterine contractions were present and after the cervix was thoroughly dilated the membranes were ruptured, a version done and the small child extracted without difficulty. Considerable bleeding followed the delivery of the placenta which seemed to be controlled, however, by the injection of 1 c.c. of pituitrin. Soon after the patient was returned to bed, bleeding began again and several clots were expelled. A careful examination was made as the patient was not yet out of the anesthesia, but no cause for the hemorrhage was found and no further bleeding occurred. The patient, however, did not rally. The pulse was weak, less than 100, and there was no response to cardiac stimulation. Within an hour the patient's condition suddenly grew worse and the picture was that of sudden death from embolism. No autopsy was permitted. The baby weighed three and one-half pounds,

cried feebly, and died a few hours later. The placenta was thick and showed marked fatty degeneration.

In this case the shock of the delivery undoubtedly contributed to the fatal ending, and I believe a better outcome would have attended the use of palliative measures.

28. *Diabetic Coma Diagnosed as Eclampsia.*—The patient, a para-i, six months' pregnant, was admitted to the hospital in a condition of coma which was diagnosed by her attending physician as due to eclampsia. The patient had not been under careful observation, and the previous history was uncertain but evidently no satisfactory urinalyses had been made. The woman was a small, emaciated-looking person with parched lips and tongue, breathing stertorously, but had none of the usual earmarks of a woman who had had either a convulsion or was the subject of a coma usually associated with eclampsia. The urine on admission, showed about 4 per cent of sugar, with a trace of albumin, no casts and a high specific gravity, together with well-marked acetone and diacetic acid reactions. Alkaline therapy was at once instituted. The patient recovered partially a few hours later and manifested an intense thirst. After a preliminary period of starvation she was given fats and proteins together with six drams of soda bicarbonate daily. The blood-sugar after fasting was 0.4 per cent. Slight improvement was noted during the next few days and the patient became quite rational. The urinary and blood-sugar determinations showed a decrease. It was difficult to examine the patient, who became more or less irrational and then went into labor, delivering herself spontaneously of a small, slightly macerated fetus of about six months' gestation. Soon after labor the condition of coma returned and no response to treatment was secured, death coming on within forty-eight hours after delivery.

This case is probably a duplicate of many others in which a diagnosis of eclampsia is made from the presence of coma with occasional convulsions before a urinalysis shows the true condition of affairs. The sudden loss of consciousness in diabetics is not unusual, particularly in pregnancy, where the disease is apt to make rapid progress.

29. *Numerous Eclamptic Convulsions with Recovery after Sedative Treatment.*—The patient, a primipara, in the seventh month of her pregnancy, was found unconscious on the floor of her apart-

ment. She had evidently had many convulsions, as the tongue was greatly lacerated and there were numerous bruises over the body. While in the act of transferring the patient to the hospital she became increasingly restless and it was difficult to restrain her. More than a grain of morphin was given by hypodermic before she became quiet. Irrigations and packs were then instituted, but the convulsive seizures during the next twenty-four hours totaled seventeen. A gradual improvement took place, and a week later the urine had cleared up sufficiently to present merely a trace of albumin with a few casts. The puffiness of the face and hands was gone and the patient was able to sit up in bed. The eliminant treatment was kept up, however. Fetal movements and heart sounds were noted for a week after admission, when they ceased, and at the close of the second week labor came on spontaneously. The patient was in the midst of a pack when she called to the nurse who, on lifting the blankets, found the fetal head had already been expelled. A poorly-nourished, macerated fetus was expelled, followed by a thick placenta with numerous areas of fatty degeneration and infarct formation. The patient then made an uninterrupted recovery.

The point of interest in this case is the large number of convulsions. As I stated, seventeen were counted after admission and the appearance of the patient showed that she had evidently had a great many before she was transferred to the hospital. The violence of the attack would have called for *accouchement forcé* or operative delivery under ordinary circumstances, but sedative treatment certainly was more satisfactory in the end than the shock of a forcible or operative delivery with a small, under-nourished child that probably would not have survived.

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